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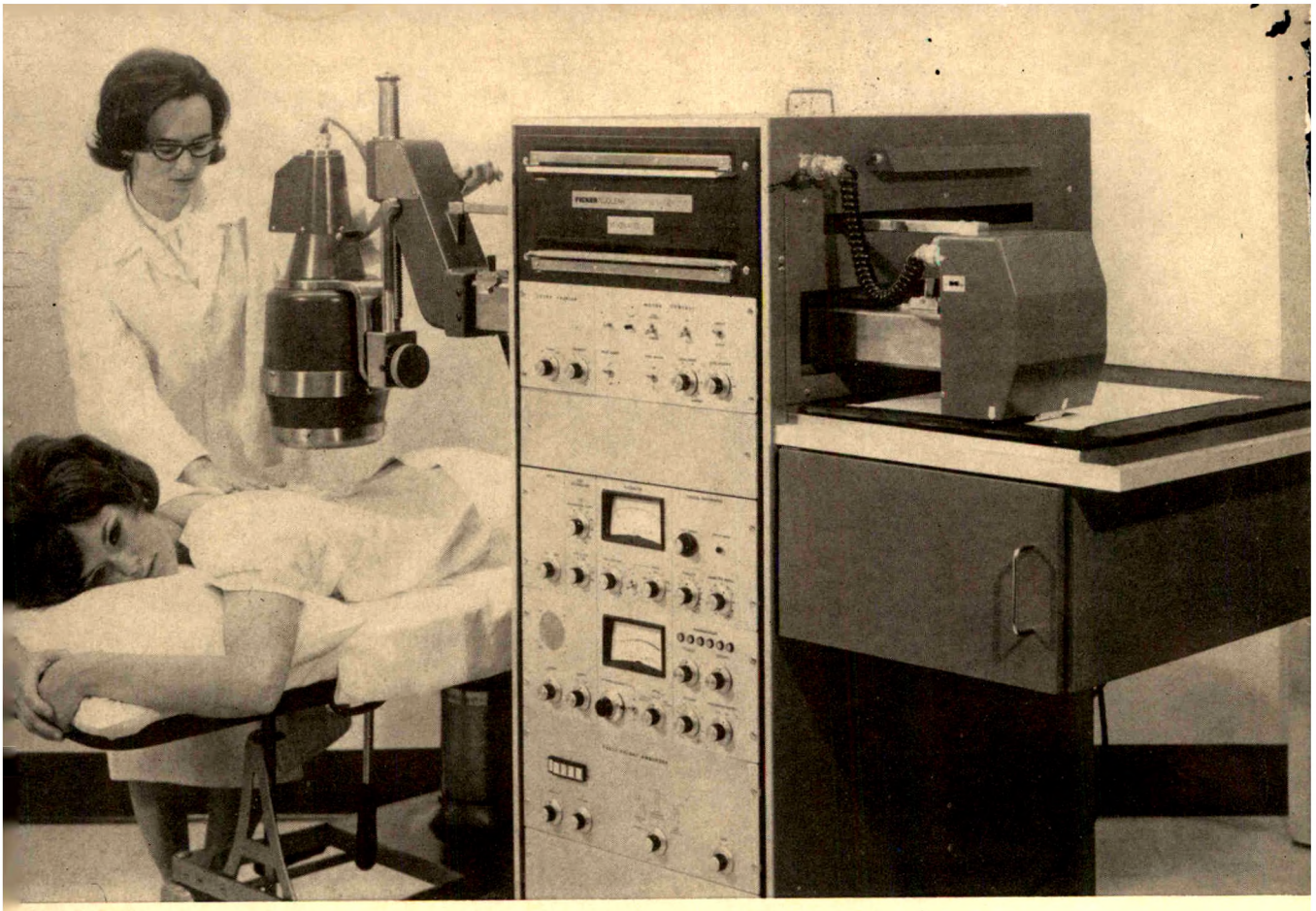
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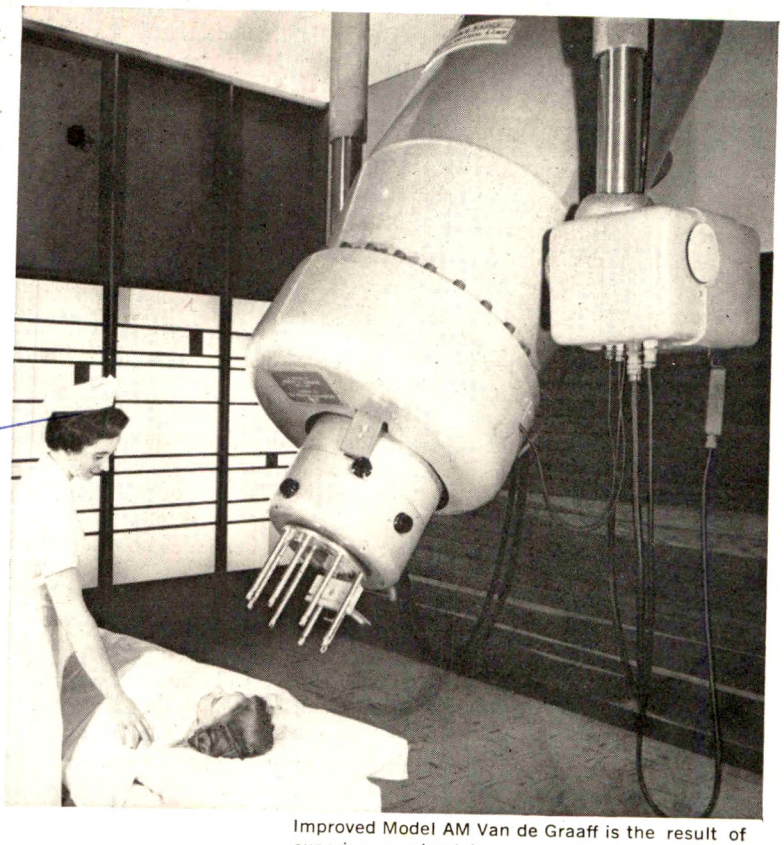
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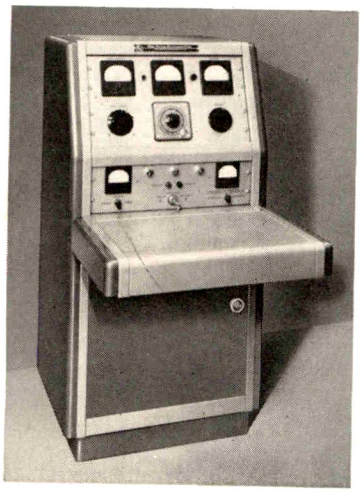


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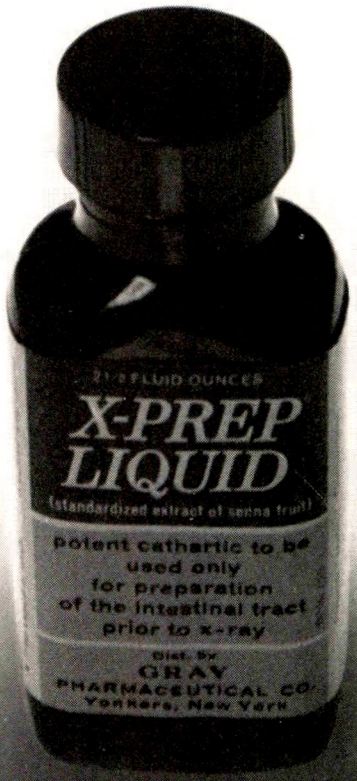
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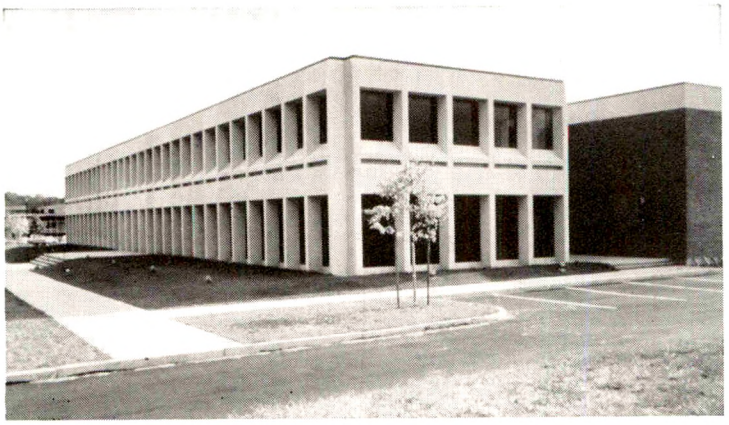


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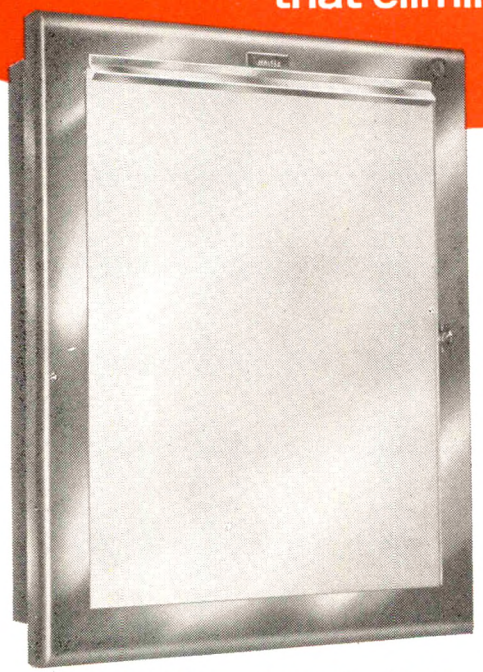
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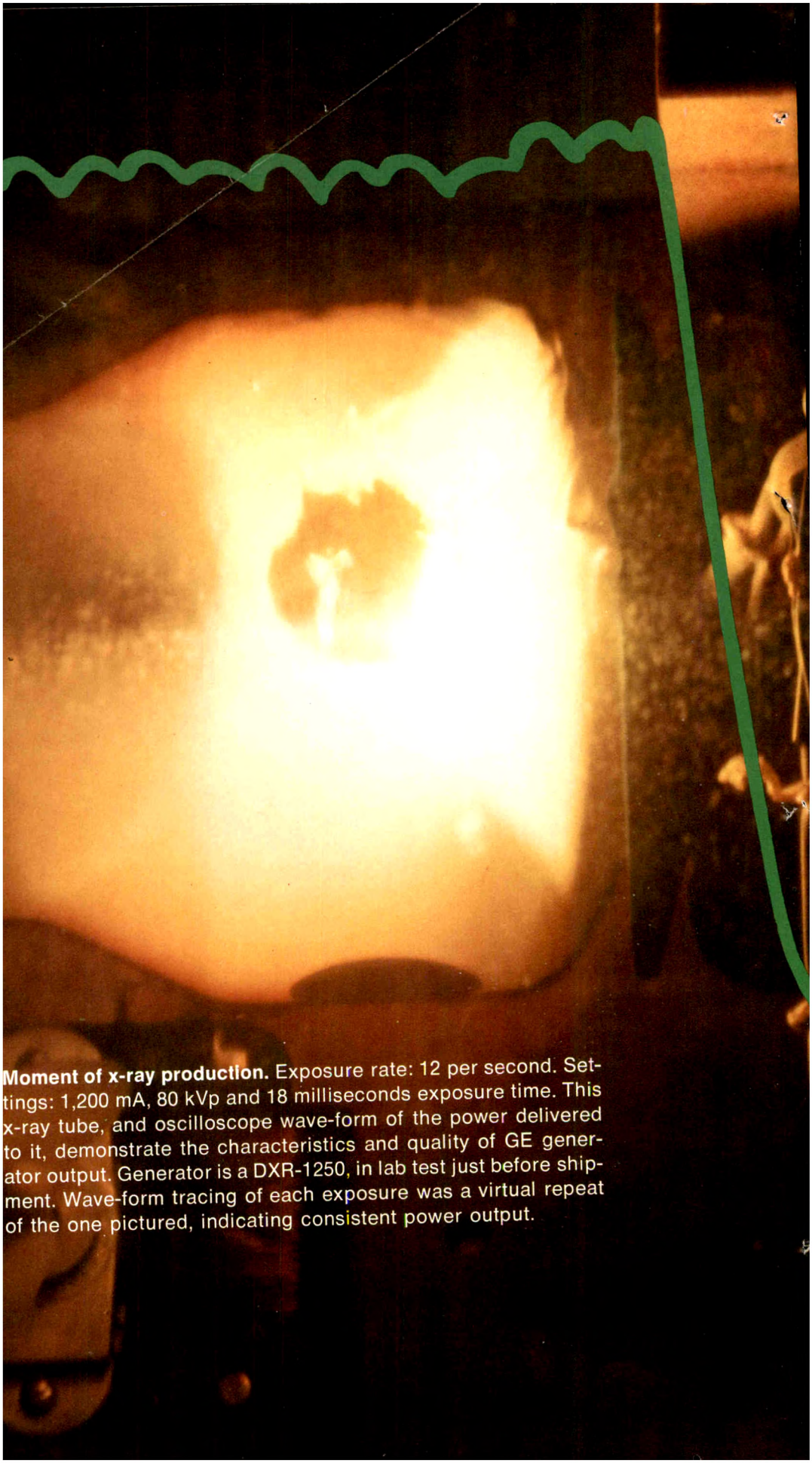
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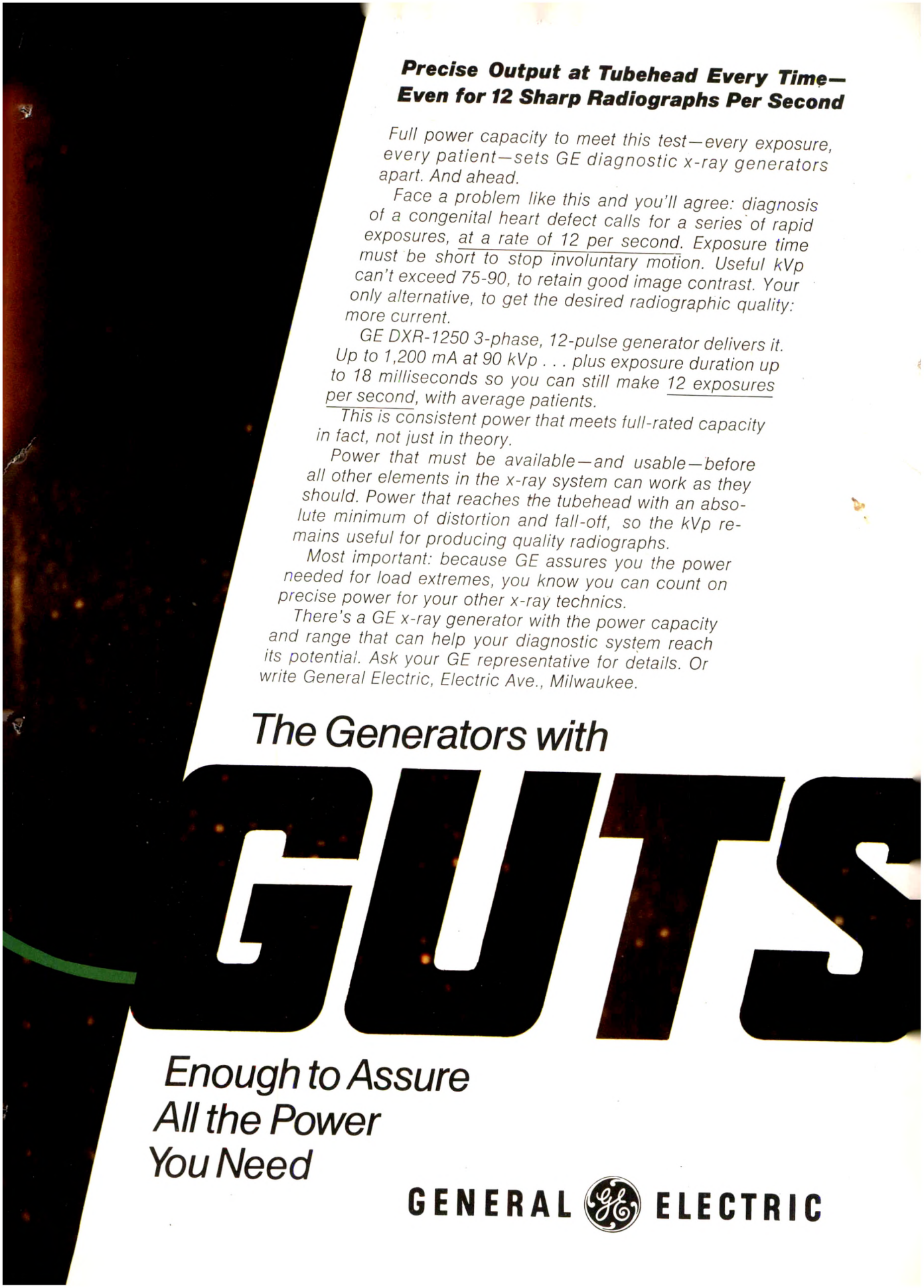
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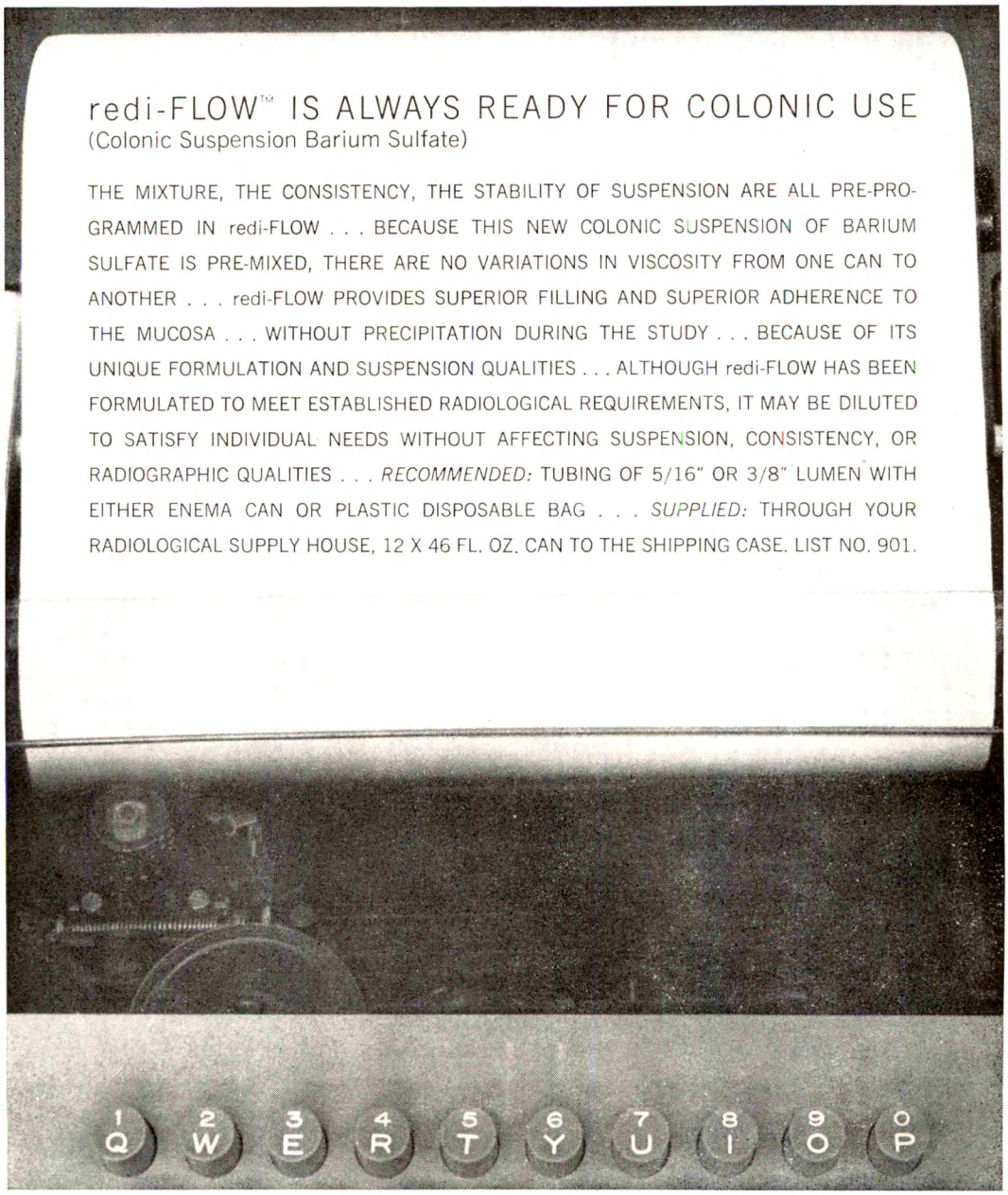
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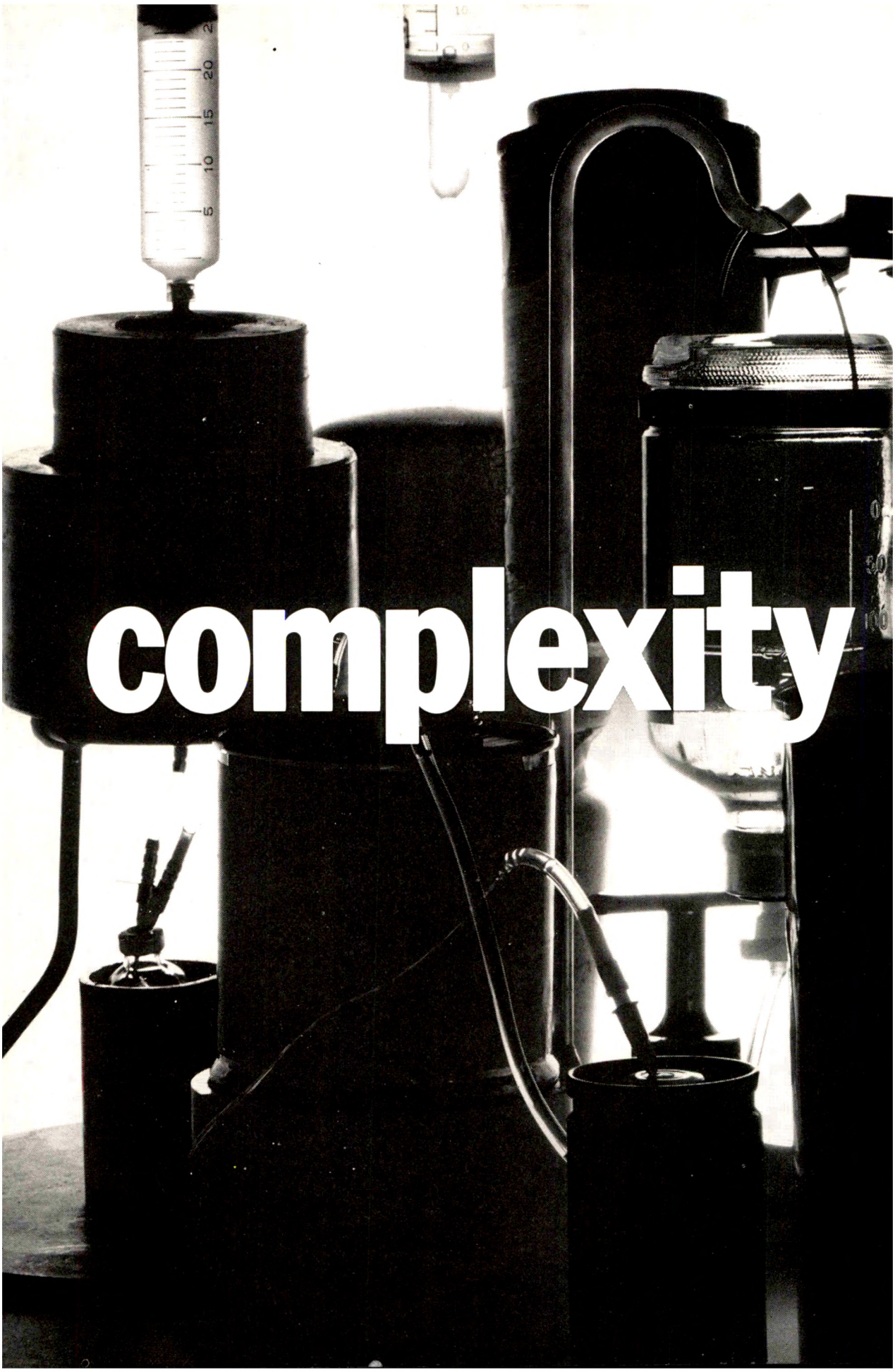
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RADIOACTIVE MATERIAL

SQUIBB

a research concept in nuclear medicine

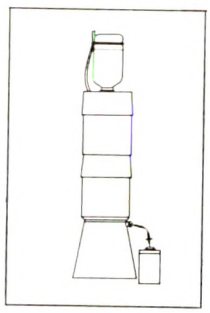
Introducing new Technetope® II

Squibb Technetium 99m STERILE GENERATOR

A FAR SIMPLER GENERATOR . . .
Hooks, hangers, and handles complicate assembly, so you won't find any on Technetope II. It's so simple that, after the usual aseptic techniques, assembly consists basically of two insertions into the generator column. Then attach an eluent bottle, an evacuated collecting vial, and milk. *That's* simplicity.

. . . DESIGNED WITH "T.D.S." IN MIND
Time: Technetope II simplicity reduces assembly time...keeping radiation exposure to a minimum. However, proper radiation safety precautions should be maintained at all times.
Distance: Technetope II allows you to keep your distance. You don't have to be constantly near the generator because it is self-milking. And eluate collection is made *at the side* of the unit—*away* from an unshielded port.
Shielding: Technetope II has another half-value layer of lead shielding—without adding a cumbersome dispenser, additional cost, or special contract.

In addition, Technetope II is readily adaptable to tandem milking which provides high concentrations of ^{99m}Tc per ml.—another Squibb first and exclusive.



Technetope II (Squibb Technetium 99m) Sterile Generator provides a means of obtaining a sterile, non-pyrogenic supply of Technetium 99m (^{99m}Tc). ^{99m}Tc, the short-lived daughter ($T\frac{1}{2} = 6$ hours) of Molybdenum 99 (^{99}Mo, $T\frac{1}{2} = 67$ hours), is obtained from the generator by periodic elution. The amount (in millicuries) of ^{99m}Tc obtained in the initial elution will depend on the original potency of the generator, while the activity obtained from subsequent elutions will depend on the time interval between elutions.

Warning: Proper radiation safety precautions should be maintained at all times. The column containing ^{99}Mo need not be removed from the lead shield at any time. The radiation field surrounding an unshielded column is quite high. Solutions of ^{99m}Tc withdrawn from the generator should always be adequately shielded. The early elutions from the generator are highly radioactive. For radiation protection, a lead shield for the collecting vial is included with Technetope II.

For additional information on this advanced generator or the tandem milking technique, please use the coupon below.

I would like to receive full information on:

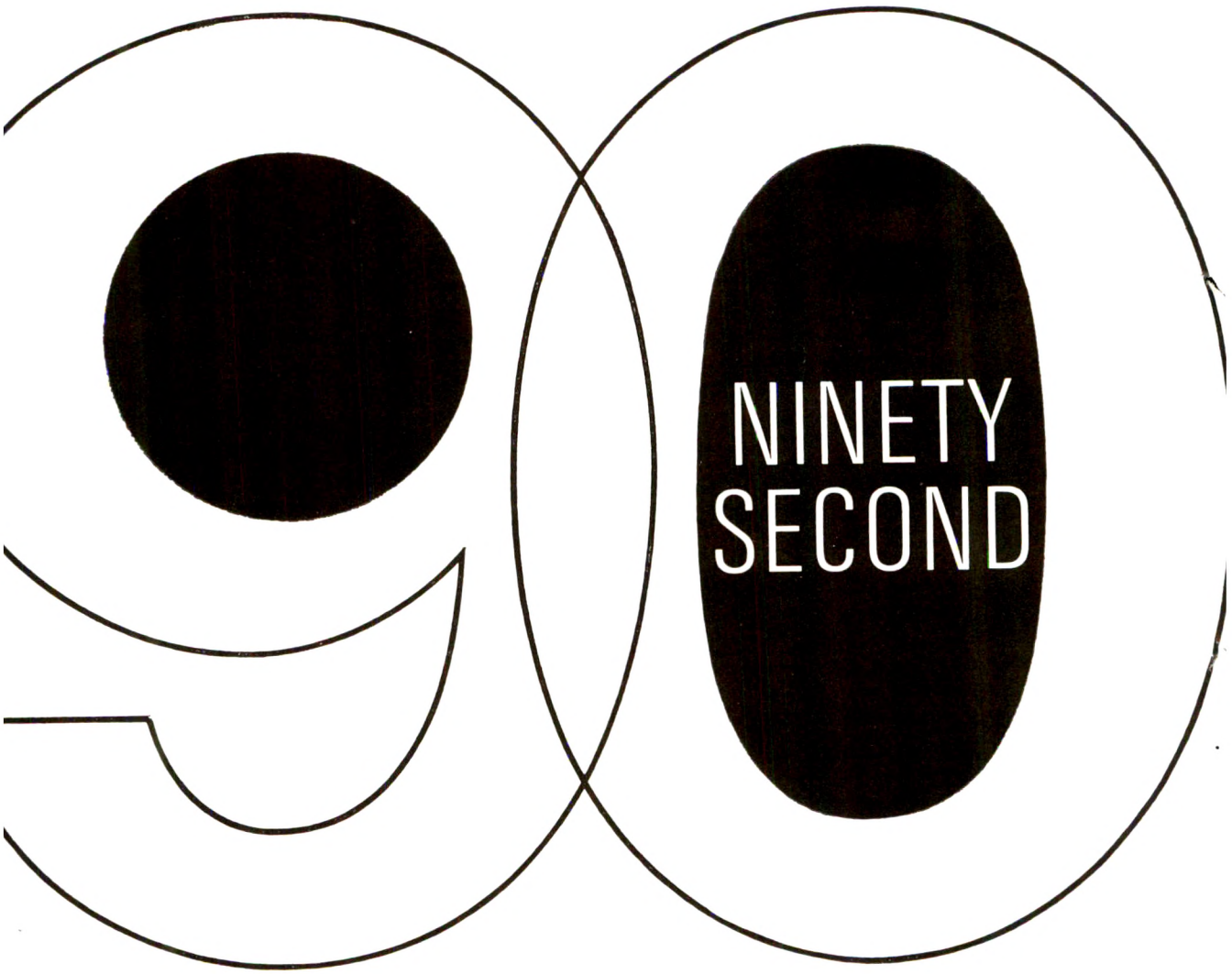
☐ **Technetope® II** (Squibb Technetium 99m) Sterile Generator

☐ Tandem Milking with Technetope II

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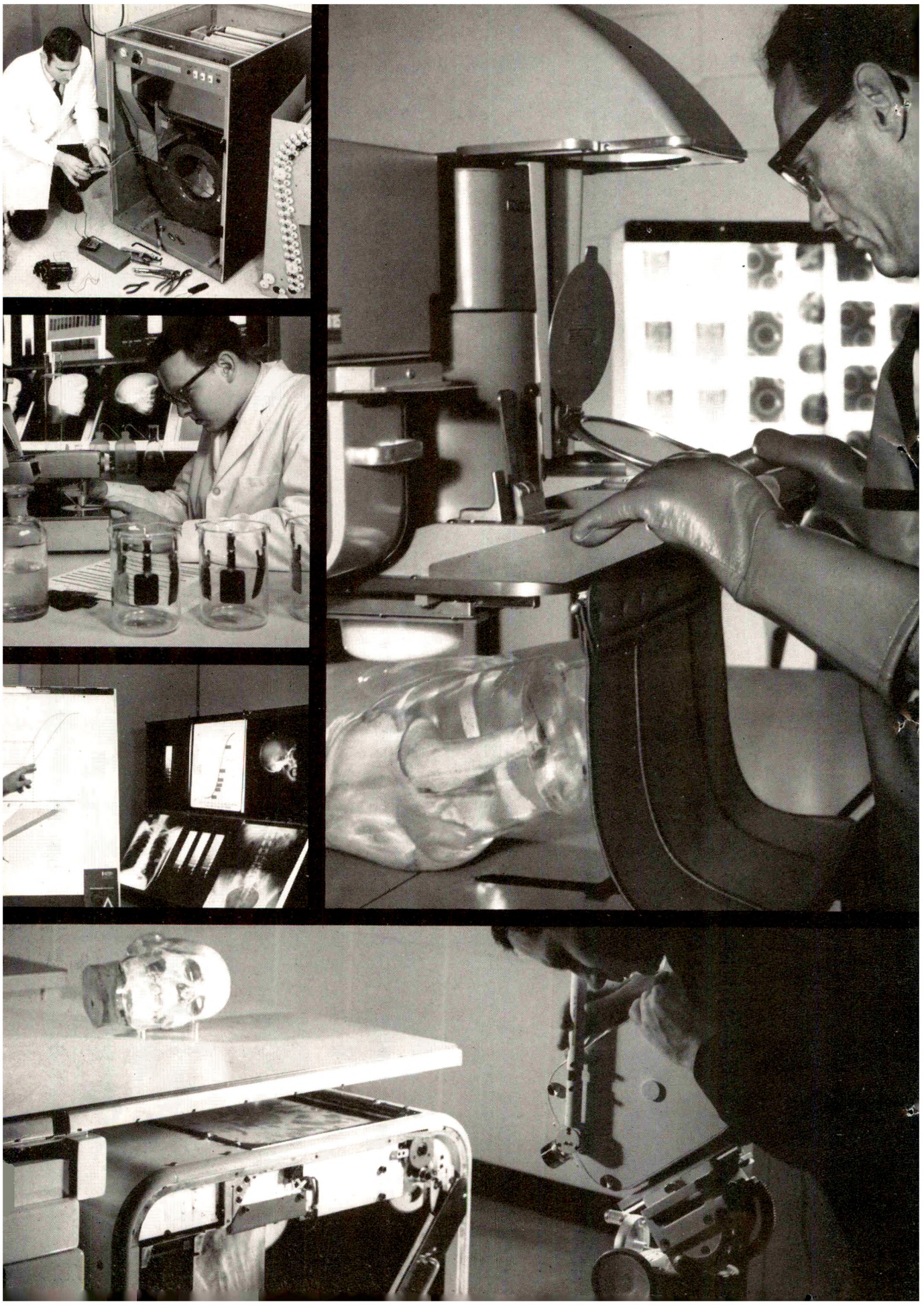
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AGFA-GEVAERT RP X-ray Film has been specifically designed for 90-second processing. Its ultra detail emulsion produces an unusually bright, fog-free image and permits rapid drying. In addition, GEVAERT RP Film has consistent characteristics resulting in quality radiographs regardless of processing cycle.

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From Du Pont's new technical service lab comes an even sharper focus on diagnostic clarity.

Here in this large ultramodern facility at Chestnut Run in Wilmington, Delaware, Du Pont scientists and technicians are at work on a variety of projects related to improving the diagnostic clarity of radiographs. Some are working on individual customer problems. Others are doing research which will bring diagnostic clarity to higher levels in the future.

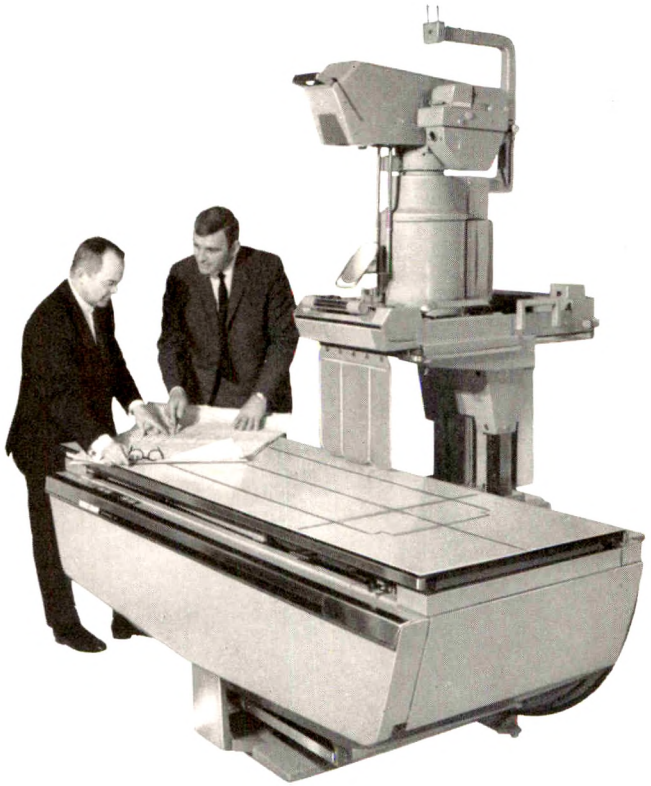
A typical day at the Chestnut Run lab might find Du Pont personnel working in any of these areas: Basic work with cine films and research to insure trouble-free performance with rapid film changers. Providing assistance with automatic processor conversions and maintenance. Specifying processing chemistry for customers confronted with unusual operating conditions. Technic refinements, such as the Du Pont Bit System and High KvP Technic. Testing archival quality of a customer's radiographs via the Du Pont hypo retention test.

The Chestnut Run lab is also the source of Du Pont technical literature and teaching seminars.

If you need help with a problem, let us focus Du Pont's science and energy on it. Ask your Du Pont TR for further details.

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Speeds up to 750 cm./minute produce simultaneous, opposed view photoscans in less than half the time required by other scanners.

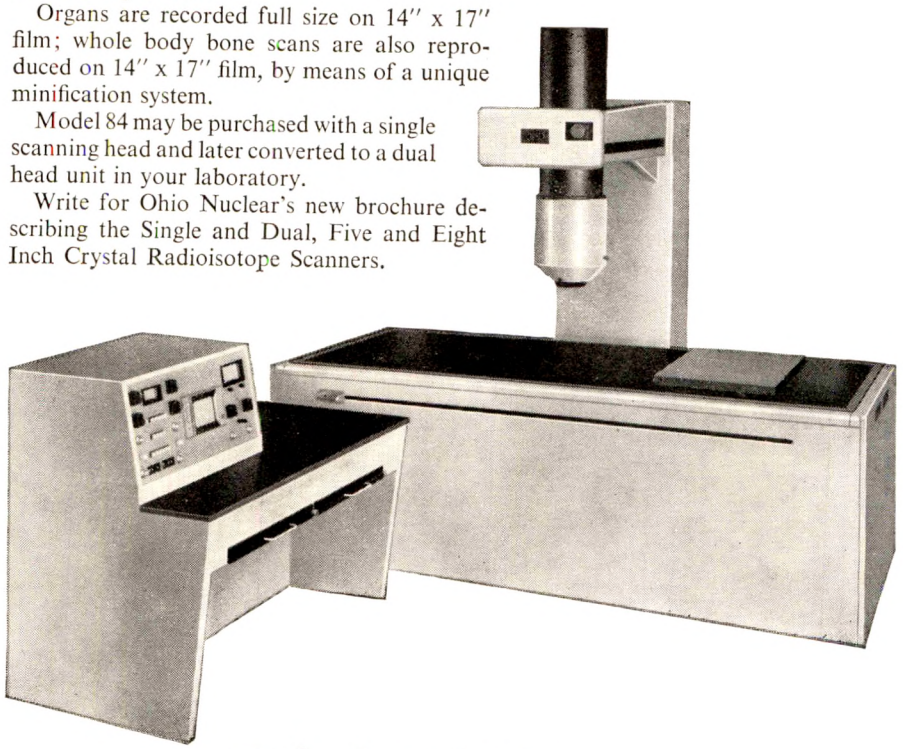
Scan progress is visually monitored on a storage cathode ray tube, which retains the organ image until manually erased.

Simplified pushbutton controls are conveniently located on the desk console. Photo Intensity Computer (PIC) circuit provides consistent, comparable maximum film density at the push of a button. Selectable levels of contrast enhancement and background erase accommodate individual preference.

Organs are recorded full size on 14″ x 17″ film; whole body bone scans are also reproduced on 14″ x 17″ film, by means of a unique minification system.

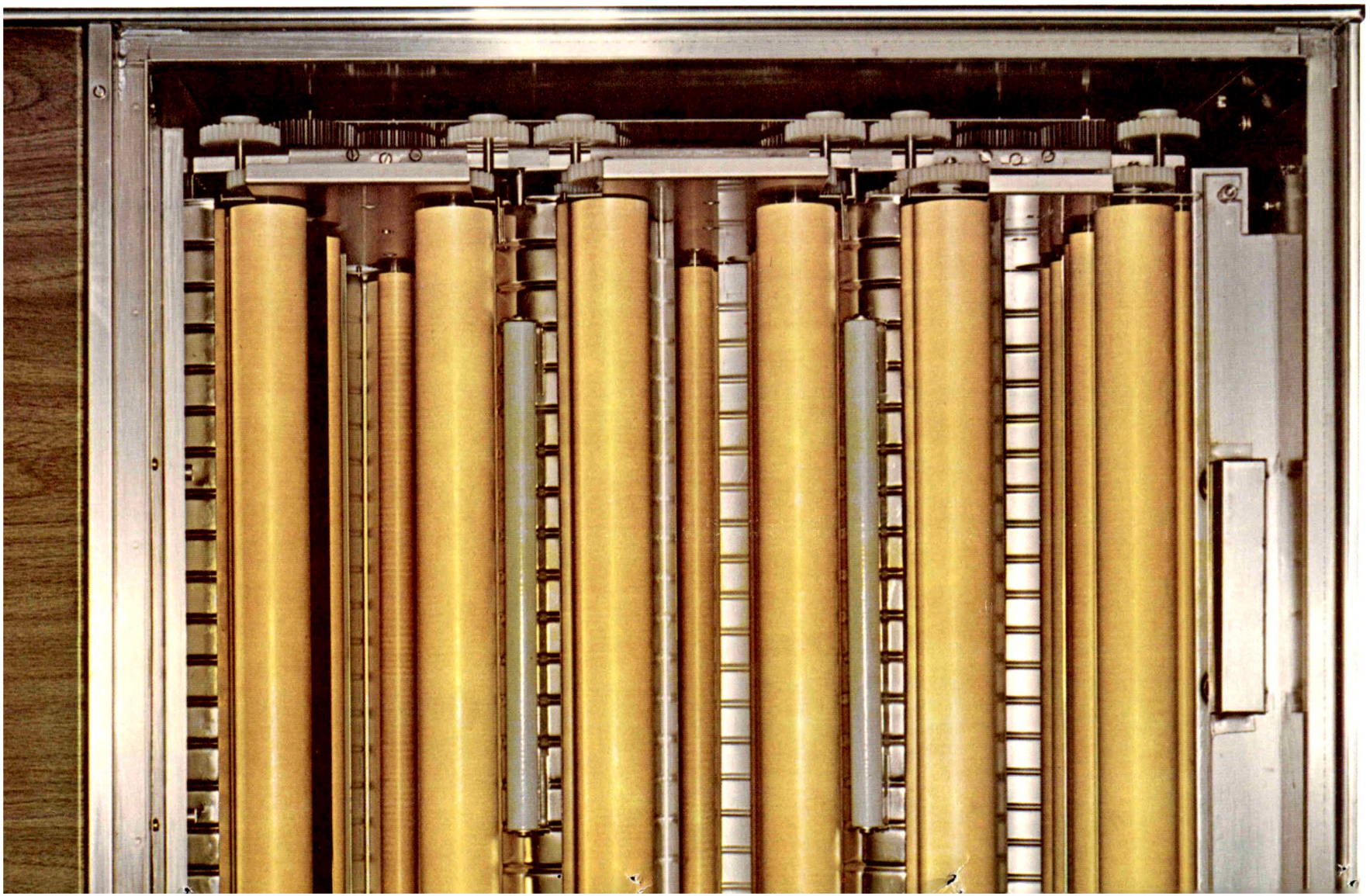
Model 84 may be purchased with a single scanning head and later converted to a dual head unit in your laboratory.

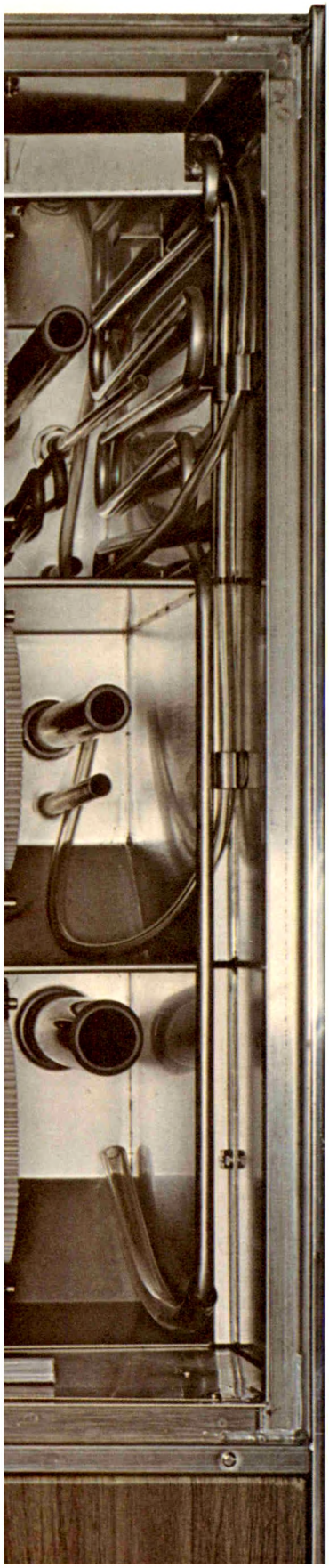
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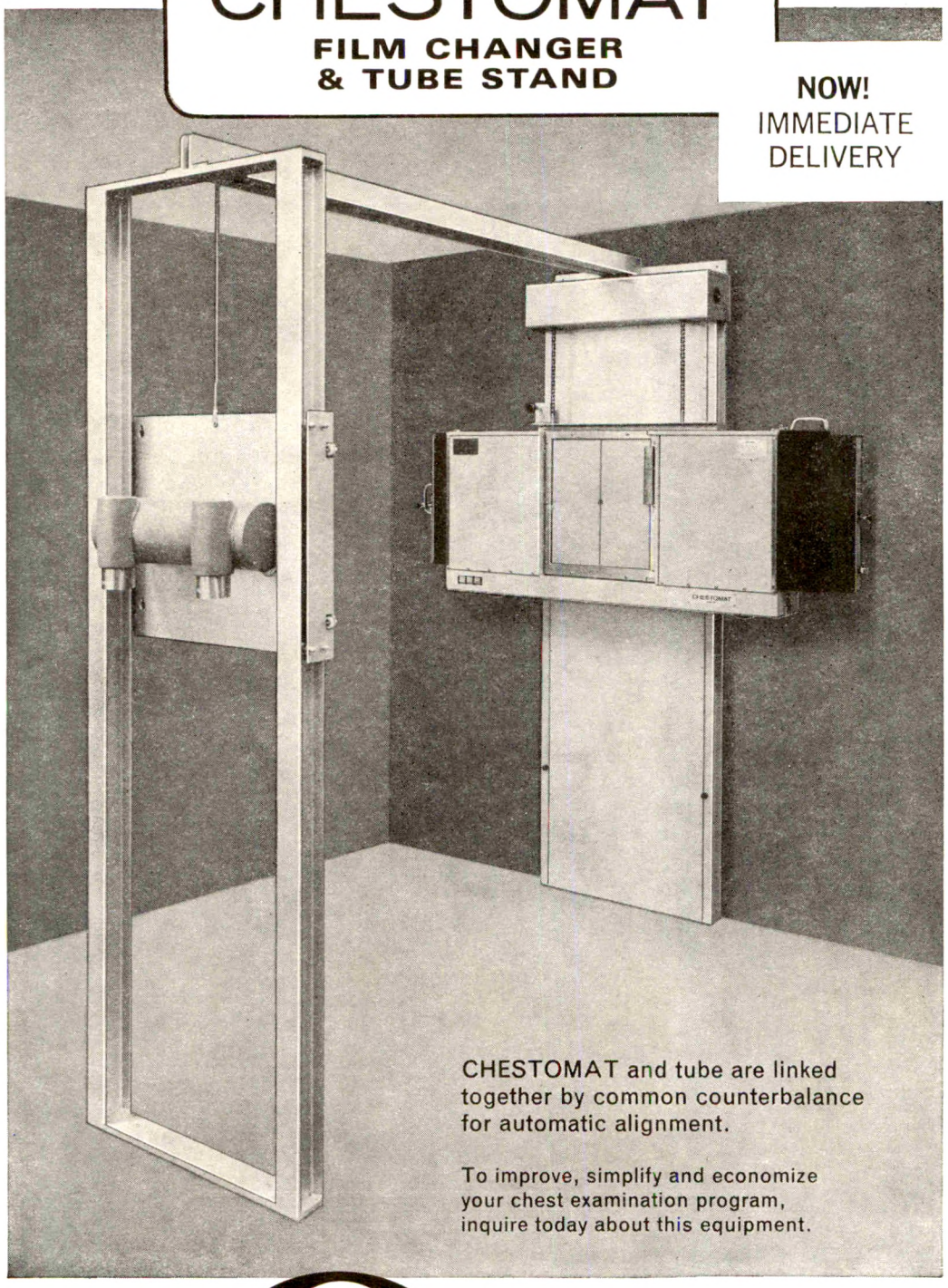
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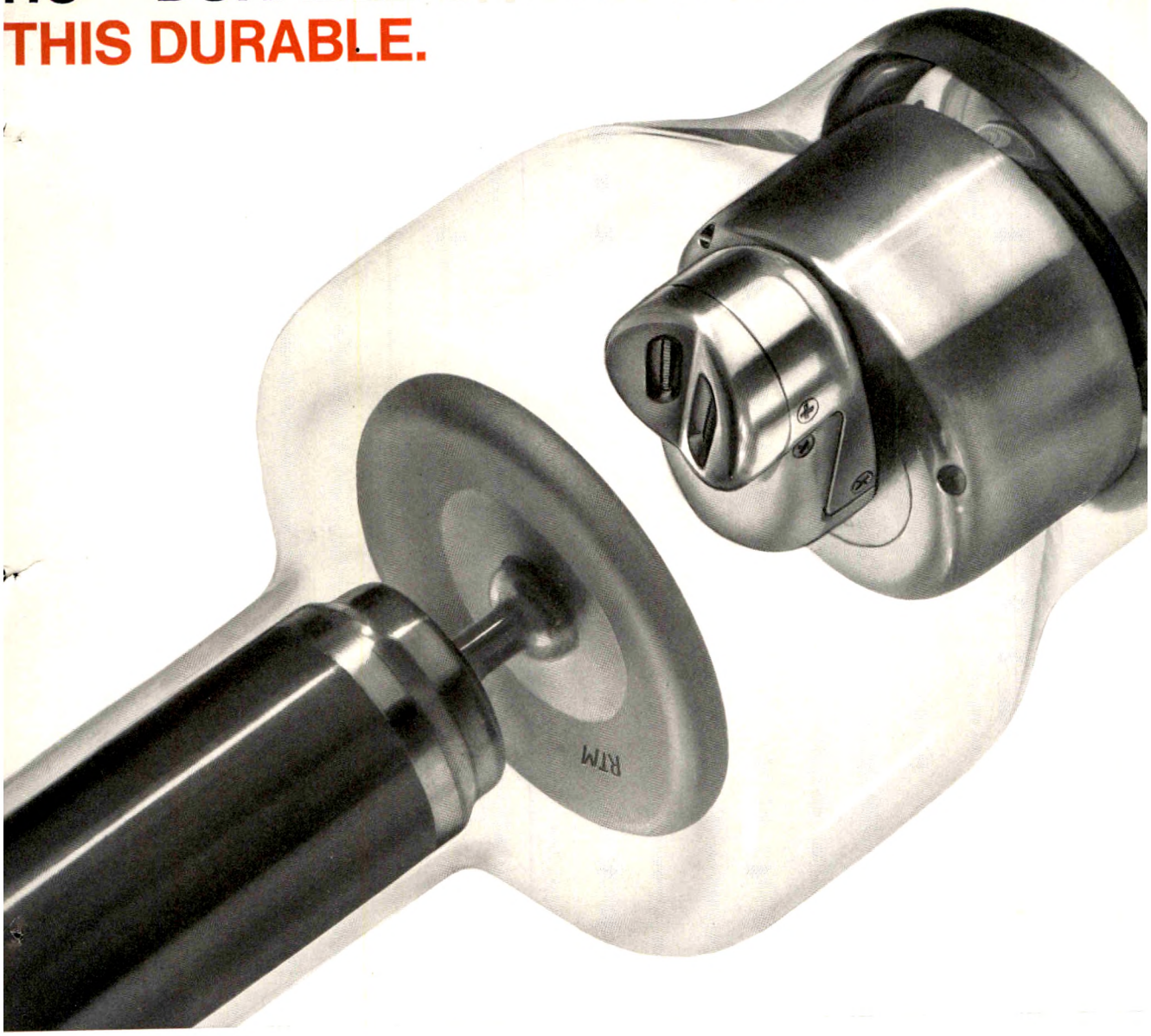
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This is Pertgen-99m, the cow that doesn't leak. Nothing comes out until you're ready to milk it.

Yields are consistent and high—an unbeatable combination!

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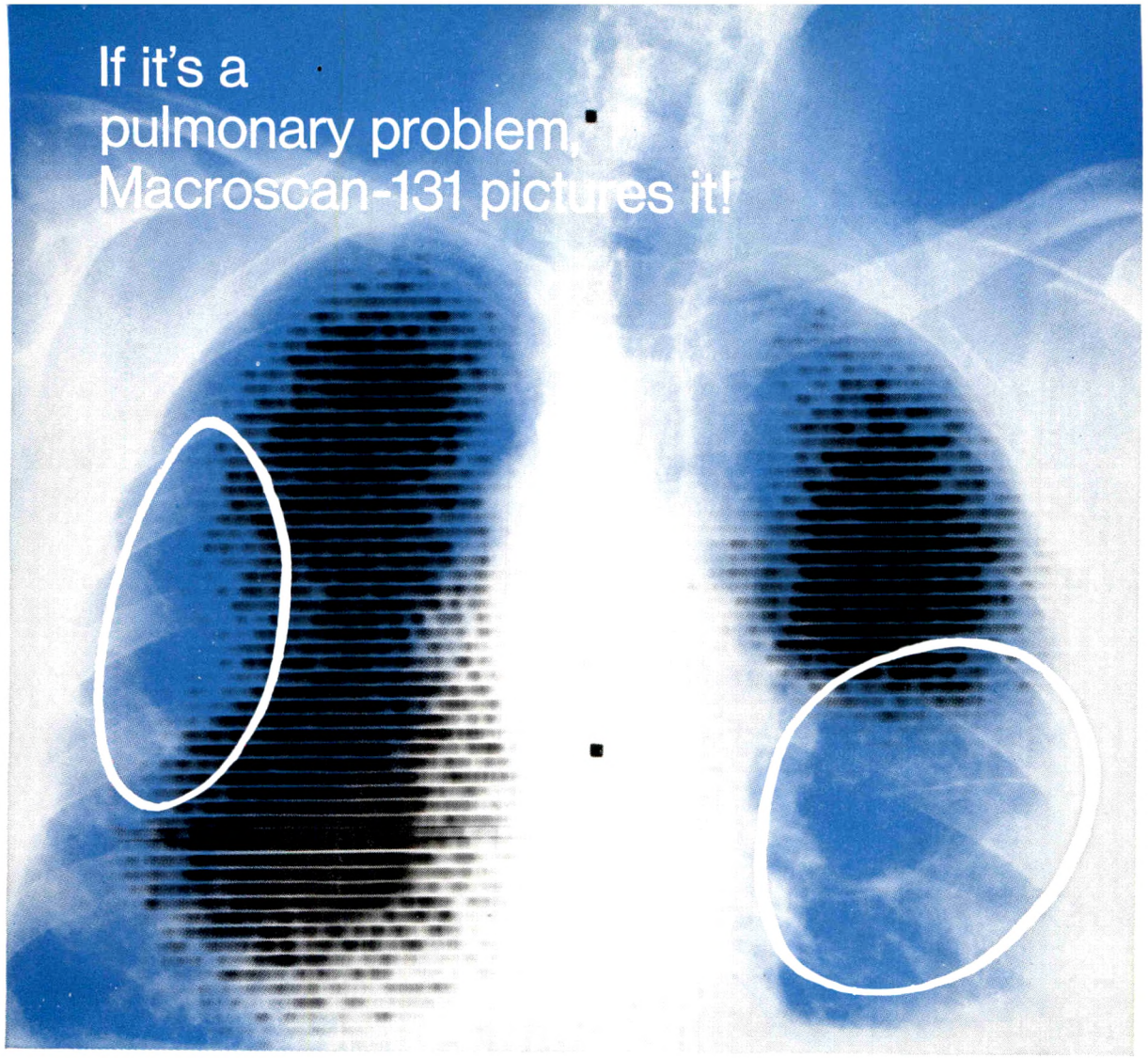
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If it's a pulmonary problem, Macroscan-131 pictures it!



A 70-year old man was admitted unconscious to the intensive care unit. Studies failed to reveal evidence of a myocardial infarction and the X-ray was not revealing. A pulmonary infarct was suspected and this diagnosis was established by a lung scan.

His posterior view scan above, showing diminished uptake in the left lingula and right lower lobe, was made with Macroscan-131. This product has many diagnostic uses:

Pulmonary embolism, suspected: To confirm (or rule out) its occurrence.

Chronic pulmonary tuberculosis: To estimate unilateral and regional function and perfusion of the lungs.

Emphysema: To evaluate the decreased regional blood flow that occurs with obstruction of vessels.

Pneumonitis: To evaluate the decreased regional blood flow that occurs without obstruction of vessels.

Lung Tumors: To evaluate the regional ischemia resulting from compression or obstruction of pulmonary arteries.

Surgery and/or other therapy for lung disorders: To evaluate the effectiveness of therapeutic measures.

Macroscan-131 is sterile and non-pyrogenic. It is ready to use and should not be heated prior to use.

INDICATIONS: For scintillation scanning of the lungs to evaluate total, unilateral, and regional arterial perfusion of the lungs.

CONTRAINDICATIONS: Radio-pharmaceutical agents should not be administered to pregnant women or to persons less than 18 years old unless the indications are very exceptional.

PRECAUTIONS, SIDE EFFECTS: Care should be taken to administer the minimum dose consistent with safety and validity of data. The possibility of an immunological response to albumin should be kept in mind when serial scans are performed. There is a theoretical hazard in acute cor pulmonale, because of the temporary small additional mechanical impediment to pulmonary blood flow. A possible case of urticaria has been related to a similar preparation. The thyroid gland should be protected by prophylactic administration of concentrated iodide solution. 903116

Macroscan™-131

AGGREGATED RADIO-IODINATED (I^{131}) ALBUMIN (HUMAN)

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We took the construction work out of barium sulfate.

We premixed it into a smooth, creamy, instantly ready esophageal contrast medium.

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Not anymore.

Now, in seconds, you can photograph your patient's esophageal tract...easily take 3, 4, even 5, plates after an initial dose. In many patients the coating of Esophotrast lasts up to 15 minutes (ample time for fluoroscopy and radiography of the esophagus and evaluation of heart size).

Now you don't have to cajole your patients into drinking cupful after cupful of barium...the 1 oz. of Esophotrast, usually all that's needed, is nongritty and fruit-flavored–a really pleasant medium to take.

And it's just a squeeze of a tube away.

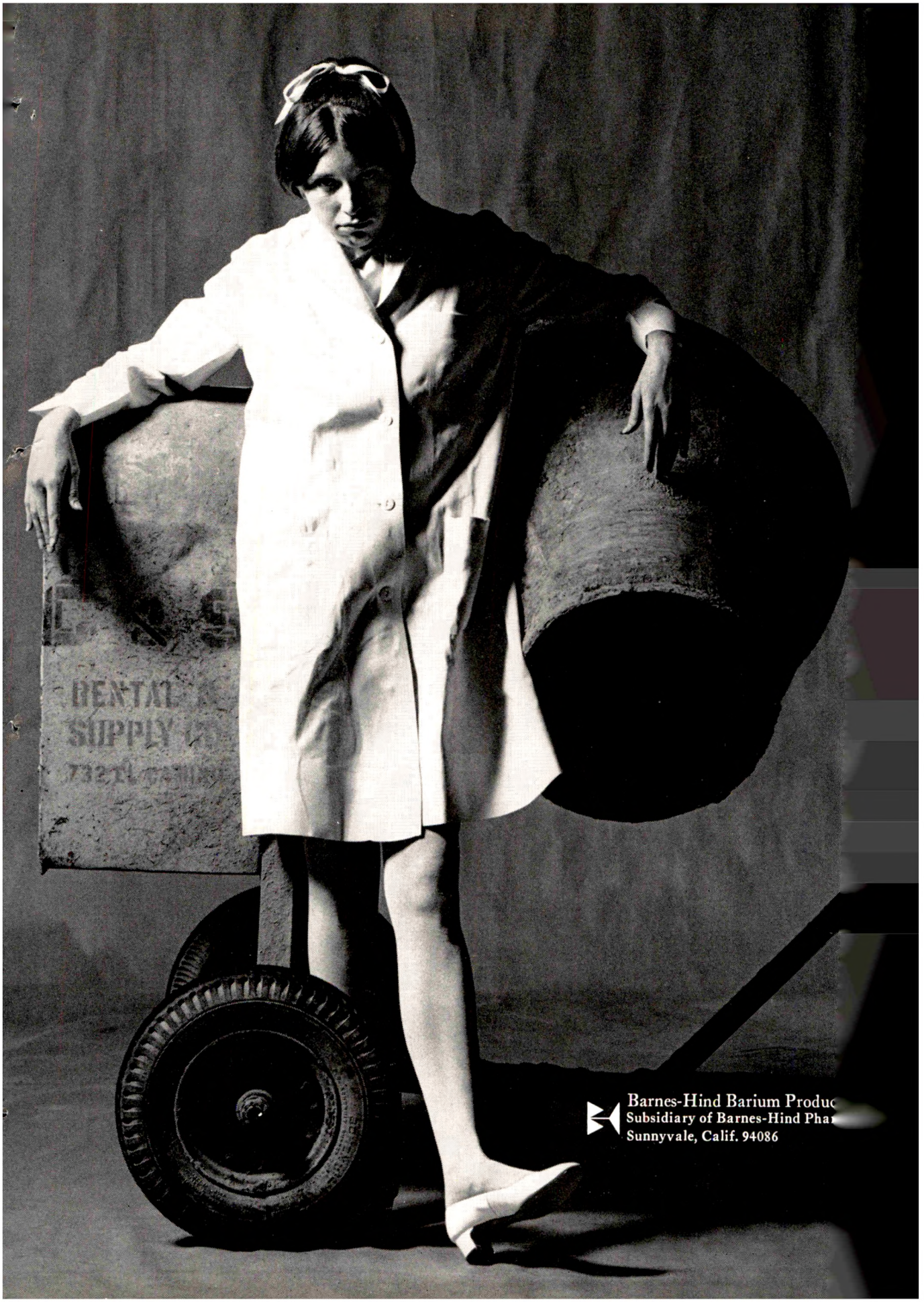
So why mix your own?

Esophotrast®

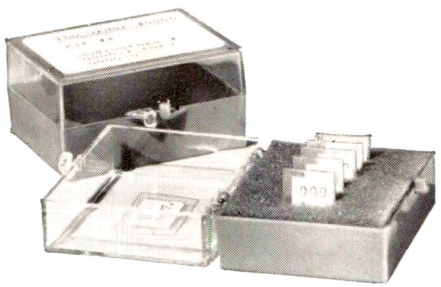
(barium sulfate)

Instantly ready esophageal cream

Recommended dose: 1 tablespoonful "chewed" thoroughly before swallowing. Repeat with a second tablespoonful to ensure prolonged adherence and coating of the esophageal mucosa.


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TLD Custom Dosimeter Service, independently and individually calibrated, now available under professionally controlled standards.



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- Dosimeters can be furnished sealed in sterile tubing.

^{6}LiF, ^{7}LiF, and CaF:Dy solid state dosimeters also available.

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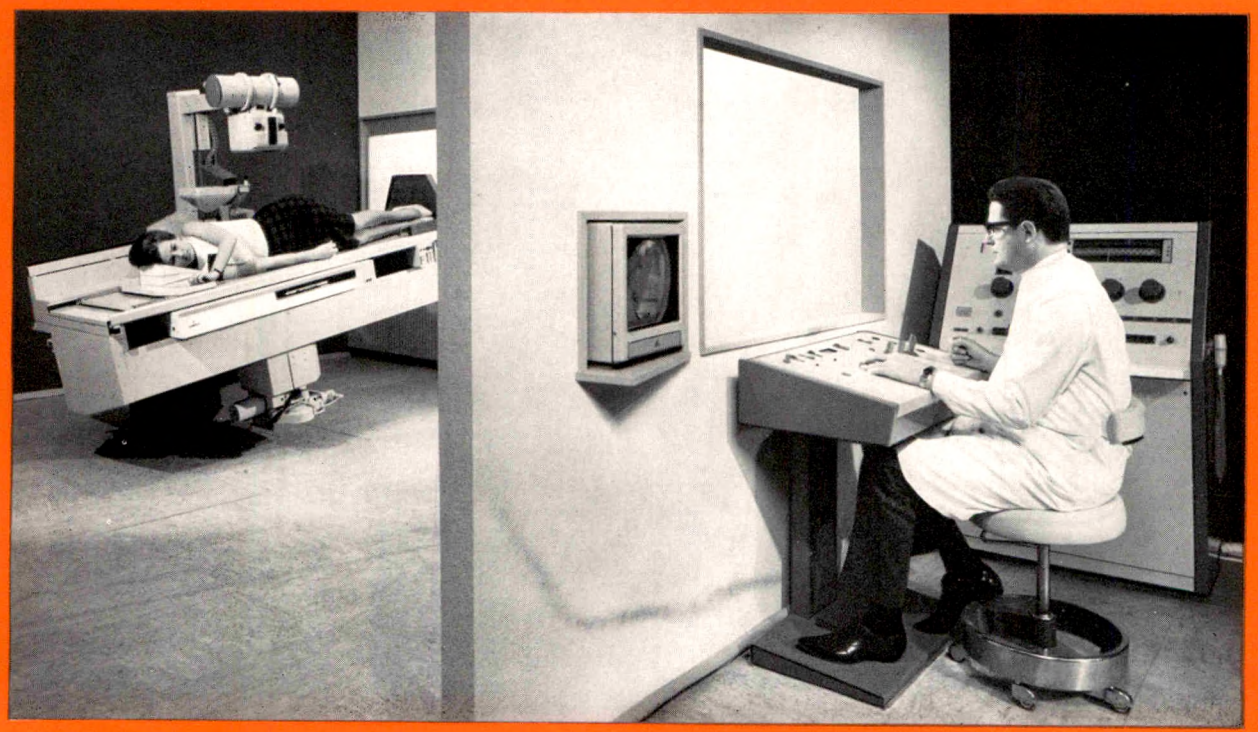
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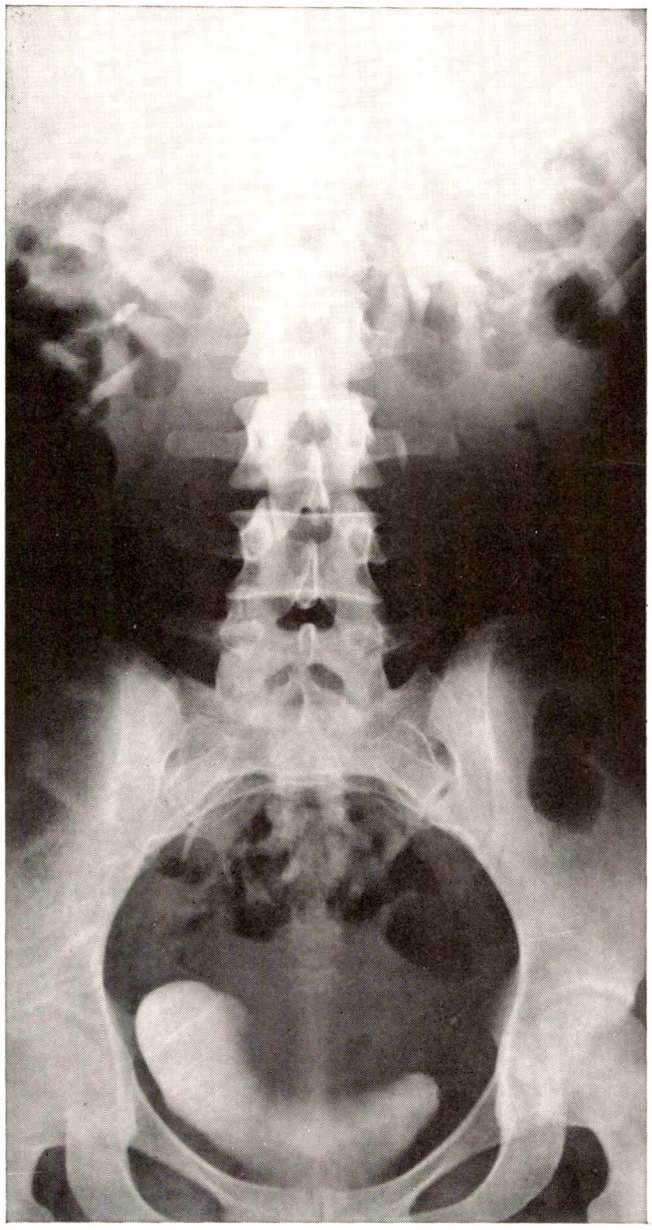
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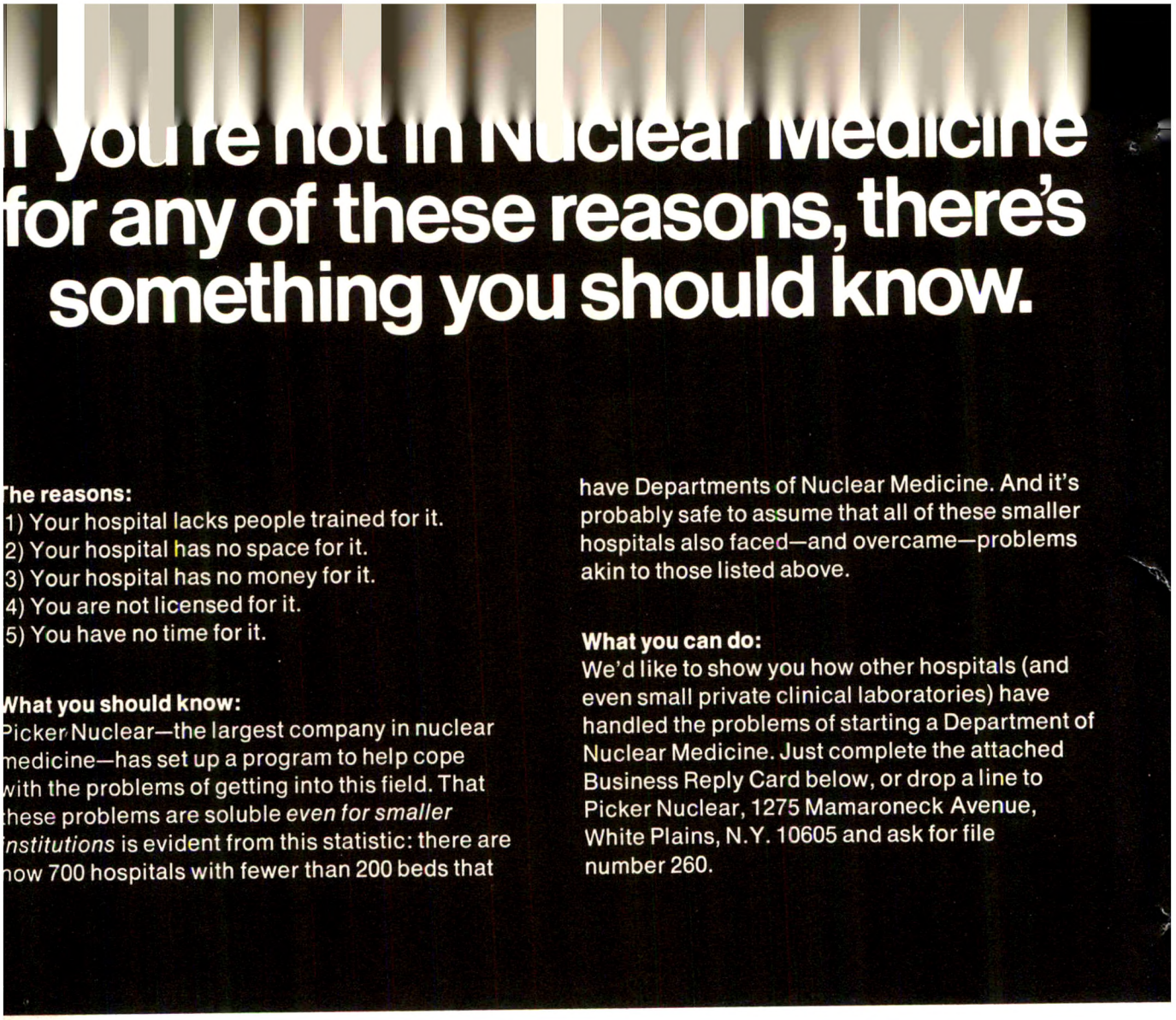
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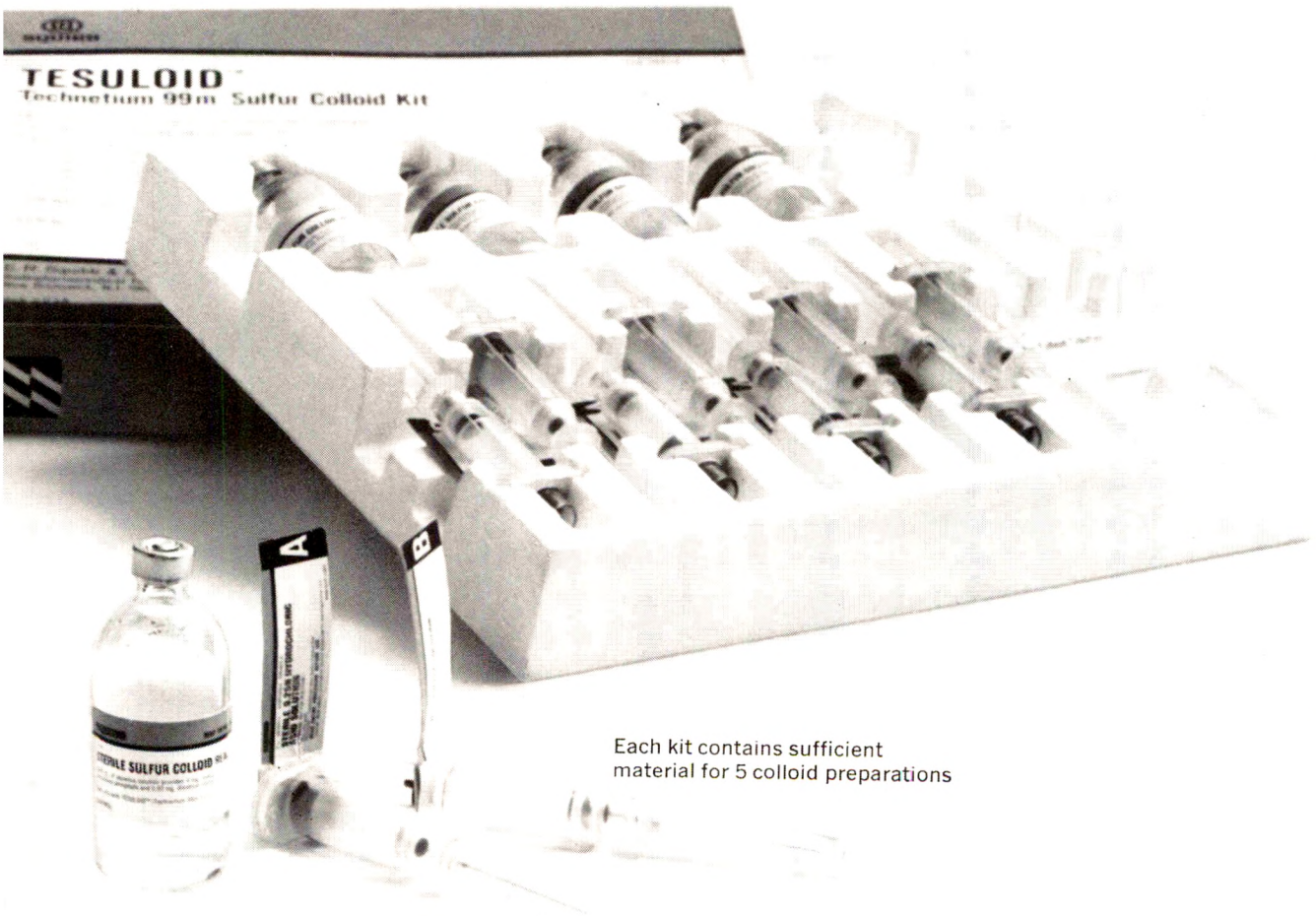
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Package contains:

5 vials (3 cc. each) Sterile Sulfur Colloid Reaction Mixture. Each cc. of aqueous solution provides 4 mg. sodium thiosulfate, 3 mg. gelatin, 8.5 mg. potassium phosphate and 0.93 mg. disodium edetate. Contains no preservative.

5 UNIMATIC® Disposable Syringes (2 cc. each) of Sterile 0.25N Hydrochloric Acid Solution. Each cc. of aqueous solution provides 9 mg. hydrochloric acid.

5 UNIMATIC Disposable Syringes (2 cc. each) of Sterile Buffer Solution. Each cc. of aqueous solution provides 35 mg. sodium biphosphate and 10 mg. sodium hydroxide.

Warning: Solutions of sodium pertechnetate ^{99m}Tc withdrawn from the generator should always be adequately shielded. Early elutions from the generator are highly radioactive.

Precaution: Radiopharmaceuticals should not be administered to pregnant women or patients under 18 unless the information to be gained outweighs the hazards.

*However, adequate shielding of the Technetium 99m—Sulfur Colloid solution should be maintained.

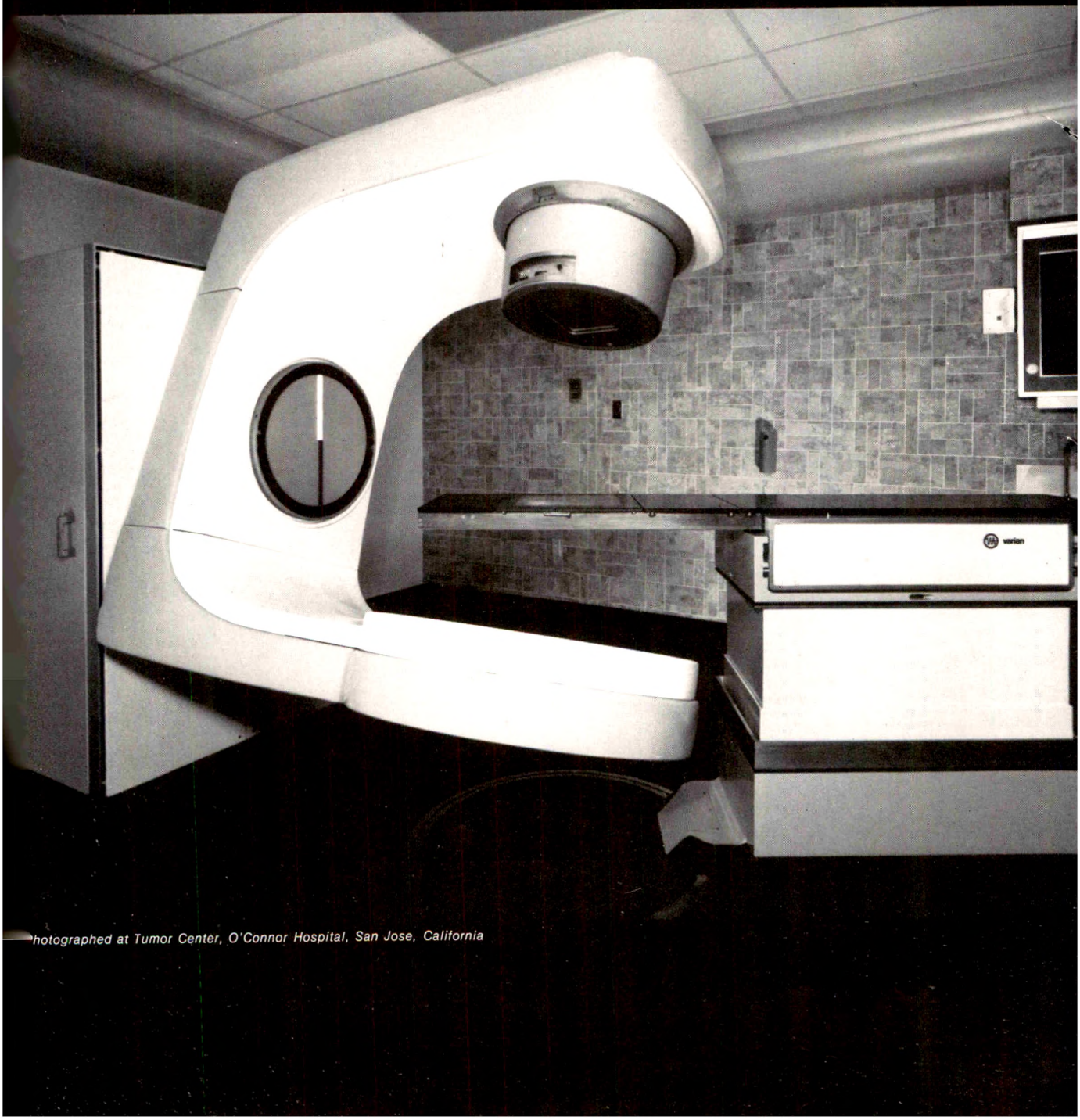
Please send me complete information on new **Tesuloid**™ Technetium 99m—Sulfur Colloid Kit.

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A simple, reliable, high-ou treatment system was.

The Clinac 4 linear accelerator was conceived to be the most ac deep radiotherapy system of our time. As an operational reality, now is fulfilling this promise. With an output of 350 Rads/min. in sizes up to 32x32 cm. Providing the uniform high intensity that e "mantle" treatments to be completed with ease in 2 to 3 minutes.

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Twenty-two Clinac 4's ar now on order. For furthe information, contact Varian Radiation Divisio 611 Hansen Way, Palo A California 94303; Spring field, New Jersey 07081; Varian A.G., Zug, Switzerland.



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Elementary Dr. Watson



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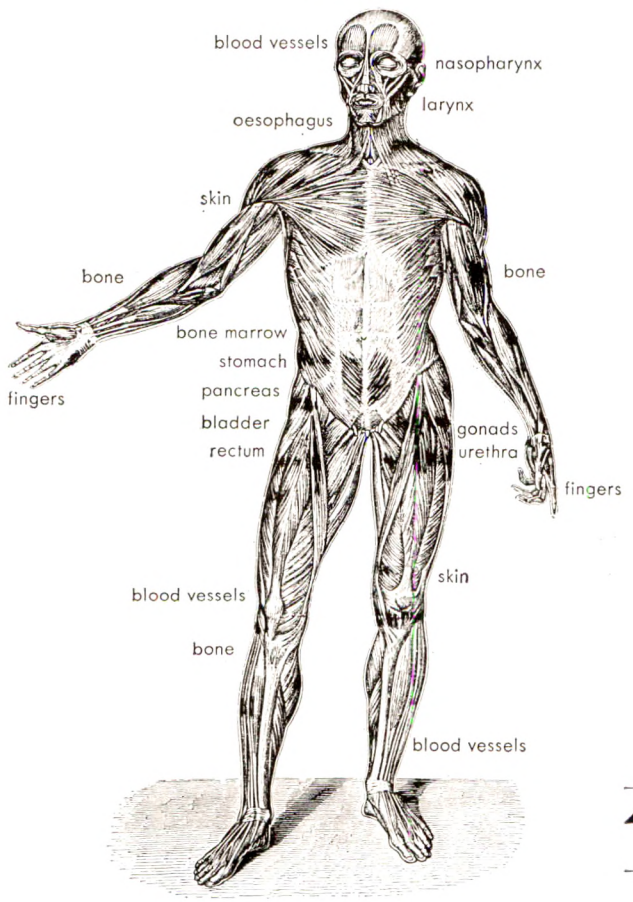
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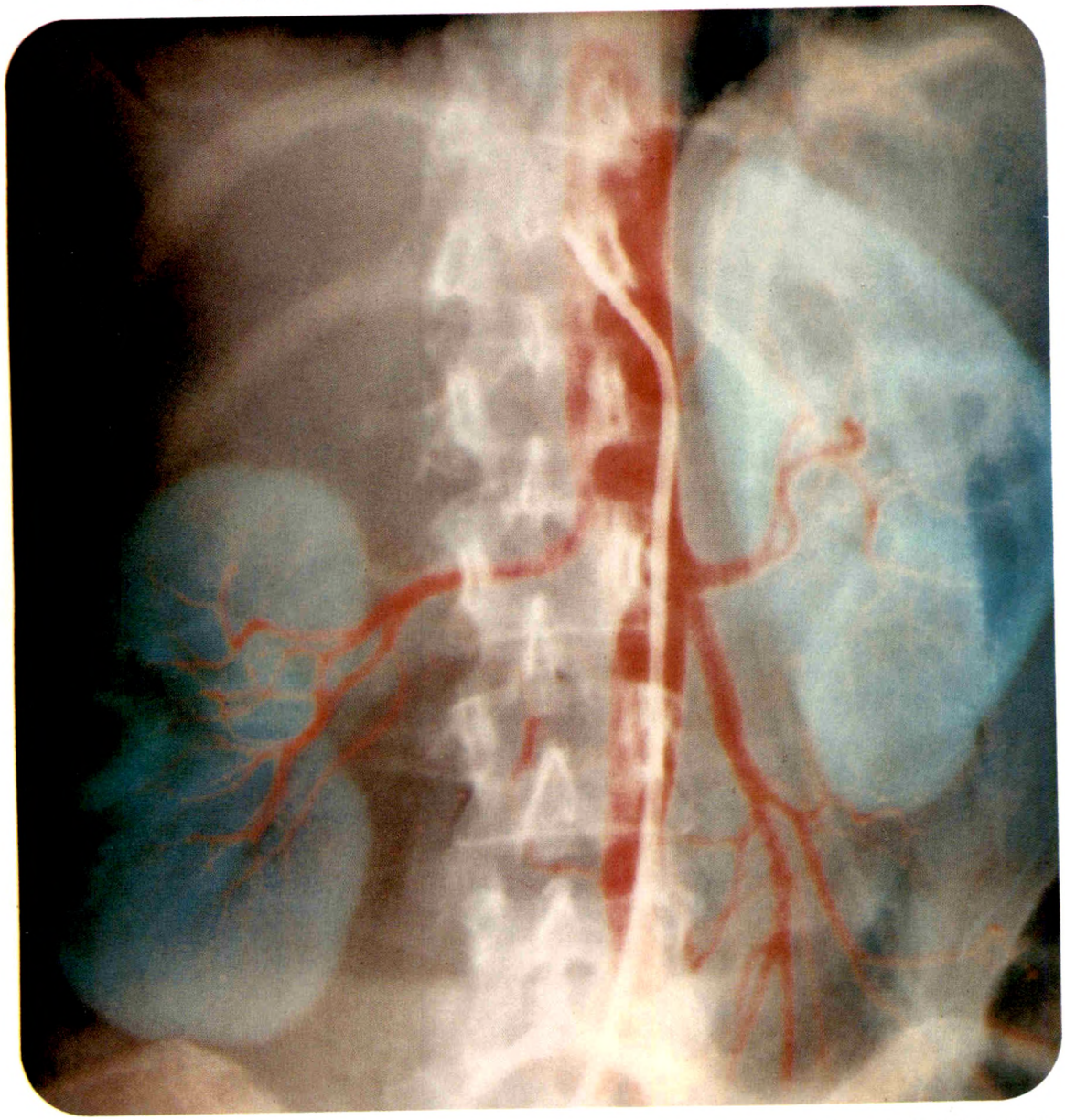
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Aortography

(percutaneous retrograde catheter technique) using Hypaque® sodium 50% as the contrast medium



The six color films illustrated, in which Hypaque was used as contrast medium, were supplied through the courtesy of Robert E. Wise, M.D. of the Lahey Clinic Foundation and New England Baptist Hospital, Boston, Mass. The technique, employing ordinary x-rays, is described in the Lahey Clinic Foundation Bulletin *14*:131, 1965.

and you'll get the same precise black-and-white definition using

Hypaque® 50%

sodium

brand of **sodium diatrizoate**

Aortography with Hypaque sodium 50% may give valuable evidence in cases of renal agenesis, duplications or ectopia, or of polycystic kidney. Aortograms are also of importance in helping to demonstrate aneurysmal change or the degree of patency of the arteriosclerotic vessel, and in aiding the surgeon to determine proper surgical management if such is needed especially where a stenotic vessel is responsible for life-threatening renal hypertension. Aortograms with Hypaque 50% have provided clearly defined needed evidence of pathology prior to surgical intervention.

Please read the summary of prescribing information on the last pages of this unit.

Excretory Urography

using Hypaque® sodium 50% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque® 50%

sodium

brand of **sodium diatrizoate**

Excretory urography with Hypaque sodium 50% provides the detection of urinary tract lesions, without interference with functional activity, without age limit and without anesthesia—important advantages when instrumentation is undesirable.

Cerebral Arteriography

using Hypaque® sodium 50% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque® 50%
sodium
brand of **sodium diatrizoate**

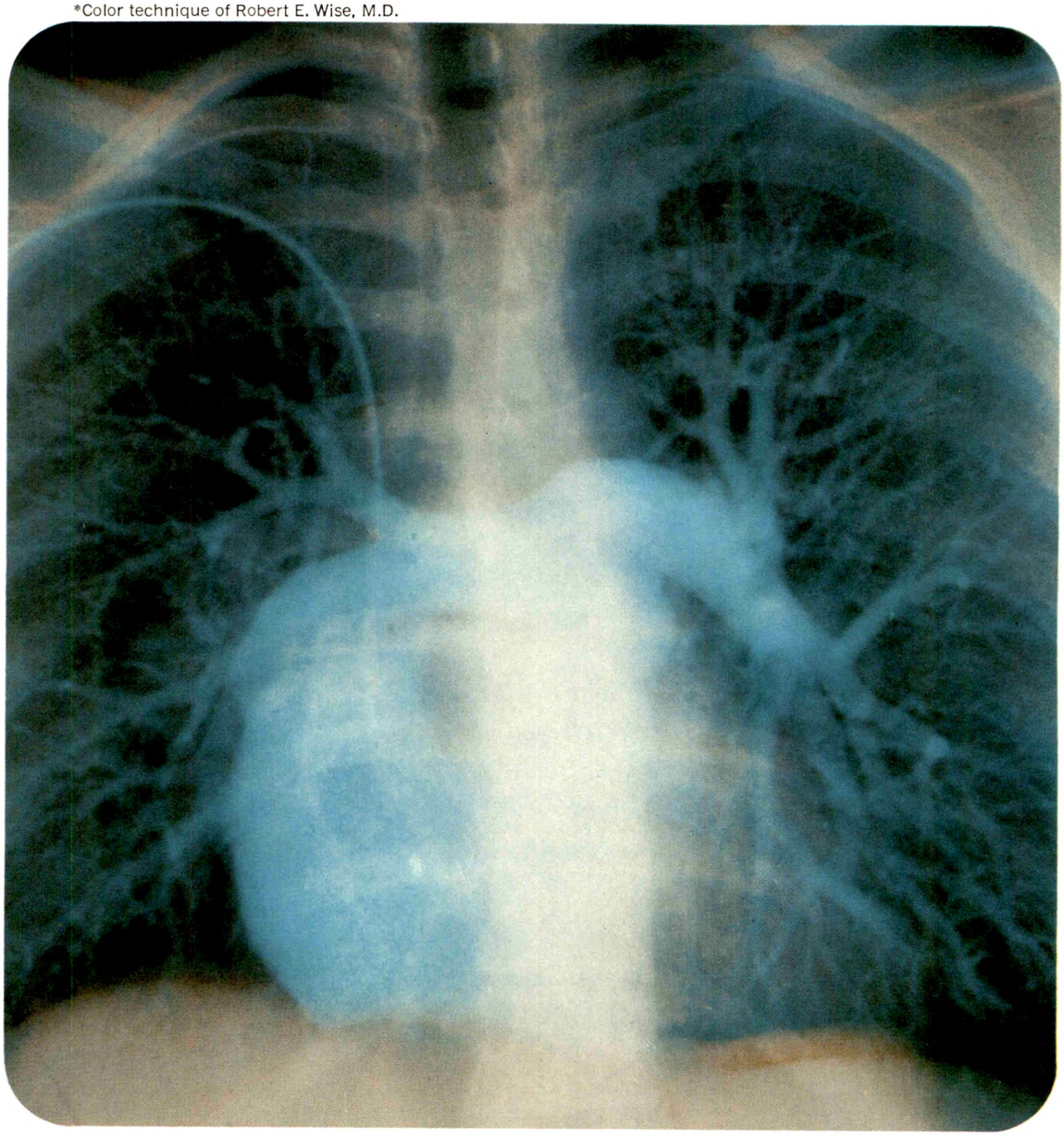
Cerebral arteriography with Hypaque sodium 50% has proved most useful in localizing and identifying intracranial lesions. Because it demonstrates both pathologic anatomy and physiology in such disorders as aneurysms, hematomas, angiomatous formations, meningiomas, glioblastoma multiforme, and other neoplasms, this procedure may provide diagnostic information frequently unobtainable by other means.

Please read the summary of prescribing information on the last pages of this unit.

Angiocardiography

using Hypaque®-M, 75% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque®-M, 75%

brand of **sodium and meglumine diatrizoates**

Because the cardiac chambers and great blood vessels of the thorax can be effectively visualized with Hypaque-M 75% (90% may be used alternatively), it provides an invaluable aid in the diagnosis of a variety of congenital and acquired cardiac defects. Angiocardiography has also proved useful in the study of neoplastic and infectious diseases of the heart. Hypaque-M 75% used for this purpose is freely miscible with blood, relatively non-irritating and nontoxic in recommended dosage, and is rapidly eliminated by the kidneys.

Nephrotomography

using Hypaque®-M, 90% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque®-M, 90%

brand of **sodium and meglumine diatrizoates**

One of the newer methods employed to reveal the nature of renal lesions is nephrotomography —a combination of rapid intravenous nephrography and body-section radiography which provides precise delineation of renal parenchyma. Nephrotomography with Hypaque-M 90% is used primarily to differentiate renal cysts from neoplasms, but may also be indicated to distinguish renal from extrarenal masses and to demonstrate congenital anomalies of the kidney.

Please read the summary of prescribing information on the last pages of this unit.

Retrograde Pyelography

using Hypaque® sodium 20% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque® 20%

sodium

brand of **sodium diatrizoate**

When loss of renal function or other causes result in unsatisfactory delineation of the urinary tract with intravenous techniques, retrograde pyelography with Hypaque sodium 20% solution can provide excellent anatomical details.

Please read the summary of prescribing information on the last pages of this unit.

Unsurpassed
• CONTRAST
• TOLERANCE

Pathology precisely defined
with
Hypaque® sodium 50% and 20%
brand of **sodium diatrizoate**

50%, ampuls of 30 ml., vials of 20, 30 and 50 ml.
20%, bottles of 100 ml.

or with
Hypaque®-M, 75% and 90%
brand of **sodium and meglumine diatrizoates**

75%, vials of 20 and 50 ml.
90%, vials of 20 and 50 ml.

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NEW YORK, N. Y. 10016

Summary of Full Prescribing Information

Hypaque® Sodium 50%
brand of **sodium diatrizoate, USP**

Sterile Aqueous Injection (Weight/Volume)

Excretory Urography and Drip Infusion Pyelography

Description: Hypaque sodium is sodium 3,5-diacetamido-2,4,6-triiodobenzoate, a radiopaque medium used to delineate internal structures.

Warning: Do not use Hypaque sodium for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

General and Specific Precautions: Caution is advised in patients with a history of bronchial asthma, other allergic manifestations, or of sensitivity to iodine; these conditions represent a special risk, though not an absolute contraindication. To avoid or minimize possible allergic reactions, premedication with antihistamines may be considered. Benadryl (diphenhydramine hydrochloride) in the same syringe with Hypaque may result in precipitation. A test dose of contrast medium is not entirely reliable. Severe reactions, including fatalities, have occurred with a test dose as well as with the full diagnostic dose.

Caution is advised in patients with severe cardiovascular disease. In patients with impaired renal function and cardiovascular disease, drip infusion pyelography imposes a sudden osmotic and sodium load which can precipitate congestive heart failure. Contrast media injected into arteries or veins can promote sickling of red cells in susceptible individuals. In patients with reduced renal function, repeat of excretory or retrograde pyelography should be delayed at least 48 hours to avoid temporary suppression of urine. In preparation for excretory urography of patients with multiple myeloma, partial dehydration is not recommended, since this may predispose to the precipitation of myeloma protein in the kidney tubules. When thyroid function studies (PBI and 24-hour radioiodine uptake levels) are indicated, they should be performed *prior* to radiographic studies or several days afterwards, to avoid inaccurate results.

Hypaque sodium 50% should always be injected at body temperature.

General and Specific Adverse Reactions: Adverse reactions, usually of a minor nature, have occurred in 10-14 per cent of patients who have received Hypaque intravenously. Reactions due to *faulty technique* include hematomas and ecchymoses, following extravasation from the vein, and pyrogenic reactions. *Hemodynamic reactions* include vasodilatation with flushing, hypotension and, rarely, vein cramp or thrombophlebitis. Serious *cardiovascular reactions* include rare cases of cardiac arrhythmias (e.g., ventricular fibrillation), shock, and cardiac arrest. Transient proteinuria may occur occasionally following the injection of radiopaques and, rarely, oliguria and anuria have been reported secondary to a hypotensive reaction. *Allergic reactions* include asthmatic attacks, nasal and conjunctival symptoms, cutaneous reactions such as urticaria and, rarely, anaphylactic shock, sometimes with fatal outcome. Severe reactions may also be manifested by signs and symptoms relating to the *respiratory system* (dyspnea, cyanosis, pulmonary or laryngeal edema), or to the *nervous system* (restlessness, confusion, or convulsions). *Other reactions* include nausea, vomiting, excessive salivation, anxiety, headache, and dizziness. Infrequently, "iodism" (salivary gland swelling) from organic compounds appears two days after exposure and subsides by the sixth day. Reactions to drip infusion pyelography may not appear until some hours after the examination.

Angiography

(Peripheral Arteriography and Venography)

Precautions (See also General Precautions): Extreme caution is advised in considering peripheral arteriography in patients suspected of having thromboangiitis obliterans (Buerger's disease). Any procedure (even needling or insertion of a catheter) may induce a severe arterial and/or venous spasm. Caution is also advisable in patients with severe ischemia associated with ascending infection.

Adverse Reactions (See also General Adverse Reactions): In addition to those listed under General Adverse Reactions, are those due to arterial trauma during the procedure (i.e., needling, insertion of catheter, subintimal injection, perforation, etc.) as well as to the hypertonicity or effect of the medium; also reported are transient arterial spasm, extravasation, hemorrhage, hematoma with tamponade, injury to nerves proximal to artery, thrombosis (rare in venography; if vein is irrigated following injection), dissecting aneurysm, arteriovenous fistula, (e.g., with accidental perforation of femoral artery and vein during needling), transient leg pain from contraction of calf muscles in femoral arteriography; transient hypotension after intraarterial (brachial) injection, and brachial plexus injury with axillary artery injections.

Cerebral Angiography: Because of the special techniques required, it is recommended that Hypaque sodium be used for this purpose only by persons skilled and experienced in carrying out this procedure.

Contraindication: Carotid angiography should be avoided during the progressive period of a stroke, since this increases the risk of cerebral complications.

Precautions (See also General Precautions): Select patients for this procedure with care. Use the 50 per cent solution with caution in extreme senility (but not old age, *per se*); advanced arteriosclerosis; severe hypertension; and cardiac decompensation.

The diagnostic value of the procedure, according to many authorities, when employed early enough in locating lesions amenable to surgery, may outweigh the added risk to patients who have recently experienced cerebral embolism or thrombosis (stroke syndrome). A small number of postangiographic fatalities, including progressive thrombosis, have occurred in which the procedure did not appear to play a role.

Patients with severe cerebrovascular disease may be examined primarily by indirect methods of angiography.

Care should be exercised to avoid contaminating catheters, syringes, needles, and contrast media with glove powder or cotton fibers.

Angiography is hazardous in subarachnoid hemorrhage. In migraine, the procedure can be hazardous because of ischemic complications, particularly if performed during or soon after an attack.

Adverse Reactions (See also General Adverse Reactions): The major sources of complications are faulty technique, occlusive atherosclerotic vascular disease, repeated injections of the contrast media, and higher doses than those recommended.

Untoward reactions are mostly mild and transient, although permanent visual field defects and deaths have been reported.

Vascular reactions: flushing, vessel spasm, thrombophlebitis, and cutaneous petechiae.

Neurologic complications: transient cerebral blindness, neuromuscular disorders, convulsions, coma, hemiparesis, unilateral dysesthesias, visual field defects, aphasia, and respiratory difficulties.

Aortography

Precautions (See also General Precautions): Special caution is advised to avoid inadvertent intrathecal injection when using the translumbar technique. The incidence and severity of reactions or complications that may occur are influenced by: the care and experience with which the procedure is performed; the amount and type of medium used; the age and condition of the patient; and the premedication and anesthesia used. Since aortography is not without some danger, it should be performed only by those experienced in the technique. Wherever possible, repeated injections of the solution during a single study should be avoided.

Adverse Reactions (See also General Adverse Reactions): Renal damage and shutdown; neurologic complications such as transverse myelitis or paraplegia; cardiovascular complications such as shock, cardiac arrest or failure, coronary occlusion, arterial thrombosis, embolism, and perforation of vessels; extravasation or hemorrhage from the puncture site or retroperitoneal catheter perforation; necrosis of the intestinal wall; acute pancreatitis; deaths; diffuse cutaneous petechiae; subintimal injection and aortic dissection.

Intraosseus Venography (See General Precautions and Adverse Reactions): A general anesthetic is sometimes necessary since the method is painful. Occasionally, extravasation of the contrast medium from the needle into the soft tissue may occur.

Direct Cholangiography

Precaution (See also General Precautions): This procedure should be used with caution in the presence of acute pancreatitis, injecting no more than 5 to 10 ml. without undue pressure.

Adverse Reactions (See also General Adverse Reactions): These may be attributed to injection pressure or excessive volume of the medium, resulting in overdistention. Such pressure may produce a sensation of epigastric fullness, followed by moderate pain in the back or right upper abdominal quadrant, which will subside when injection is stopped.

Some of the medium may enter the pancreatic duct and cause a transient serum amylase elevation 6 to 18 hours later, without apparent ill effects. Pancholangitis resulting in liver abscess has been reported. Occasionally, nausea, vomiting, fever, and tachycardia have been observed.

Hysterosalpingography

Contraindications: Menstruation, active or imminent; infection in any part of the genital tract, including the external genitalia; pregnancy, known or suspected. Use not advised for six months after end of pregnancy, or 30 days after conization or curettement.

Precaution (See also General Precautions): Caution should be exercised in patients with known or suspected carcinoma to avoid possible spread of the lesion by the procedure.

Splenoportography

Precautions (See also General Precautions): Procedure should be performed with caution on patients with blood dyscrasias, a tendency to severe bleeding, or a spleen recently become tender and palpable.
Adverse Reactions (See also General Adverse Reactions): Persistent hemorrhage with hemoperitoneum has been reported, and, in some instances, hemorrhage has required splenectomy.
How Supplied: Ampuls of 30 ml., boxes of 1, 10, and 25. A 1 ml. sensitivity test ampul is furnished with each ampul. Vials of 20 and 30 ml., rubber stoppered, boxes of 1, 10, and 25. Vials of 50 ml., rubber stoppered, boxes of 1 and 10. Each vial contains sufficient excess to permit withdrawal of 1 ml. for testing sensitivity.

If the solution is chilled, crystals may form but will readily dissolve if the ampul or vial is placed in moderately hot water before use. Cool to body temperature before injecting.

Hypaque® Sodium 20%

brand of **sodium diatrizoate**

Sterile Aqueous Solution 20% (weight/volume)

Precautions: It has long been known that oliguria or anuria may rarely follow bilateral retrograde pyelography or uncomplicated cystoscopic ureteral manipulation. Various mechanisms have been proposed to explain this occurrence, such as reflex anuria, edema, and occlusion of the ureteral orifices from local trauma, pressure, manipulation, sensitivity to the radiopaque medium or to residual disinfecting antiseptic on ureteral catheters, pyelotubular backflow, transient interstitial renal edema with increased pressure, and reduced renal blood flow. Because of the possibility of acute renal failure following bilateral retrograde pyelography, some authors conclude that retrograde pyelography should be done on only one side at a time.
Side Effects: The nonirritating properties of the medium minimize the likelihood of ureteropelvic spasm; in addition, a more natural outline of the upper urinary tract is obtained because of these properties. There is also a decrease in the incidence and severity of discomfort and colic following retrograde examination. Excellent tolerance was evidenced by notably few untoward reactions. Minor side reactions, which occurred in a few patients, consisted of nausea, vomiting, excessive salivation, and sweating. There was no indication of irritation of the urinary tract mucosa that could be attributed to the medium.

With Hypaque Sodium 20 per cent, reflux into the blood stream or lymphatics (pyelovenous or pyelolymphatic backflow) as a result of undue pressure of administration is not apt to result in a generalized reaction, since intravenous injection of more than double this concentration has been well tolerated.

Hypaque®-M, 75%

brand of **sodium and meglumine diatrizoates**

Sterile Aqueous Injection 75% (weight/volume)

Caution: The 75 per cent concentration is intended primarily for angiocardiography, nephrotomography and selected cases of peripheral angiography. Hypaque sodium (brand of diatrizoate sodium) 50 per cent solution is recommended for excretory urography, cerebral angiography and most cases of peripheral angiography.
Warning: Do not use Hypaque-M, 75 per cent for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

Angiocardiography

Contraindications: Use of Hypaque-M, 75 per cent is contraindicated in patients with advanced renal destruction associated with severe uremia. Hypaque-M 75 per cent should not be used for myelography.
Precautions: 1. Caution is advised in patients with hyperthyroidism, hypertension, active tuberculosis and a history of allergy, especially to iodine. Angiocardiography and nephrotomography should be performed cautiously in patients with heart disease and circulatory failure and should not be employed in patients who are in collapse or who are critically ill or debilitated. A renal function test is advisable before administration of the 75 per cent solution.

2. Prior to the examination, the patient may be tested for sensitivity to the radiopaque medium. (See Side Effects and Sensitivity Tests.) Patients who show an idiosyncrasy should not be given the drug.

3. Premedication with a barbiturate is advisable if the patient is extremely nervous. Demerol (brand of meperidine), chlorpromazine and antihistamines have also been recommended for premedication. Such antihistamines as chlorpheniramine maleate or tripelennamine hydrochloride may be administered about 30 minutes before injection of the radiopaque medium or may be combined with it in a single injection. Many authorities recommend general anesthesia for small children and uncooperative patients.

4. Facilities for resuscitation including a mask with a breathing bag and pure oxygen should be available for immediate administration in case of severe reaction.

5. The sensations to be experienced should be described to the patient in order to allay apprehension before injection and to prevent excitement afterward.

6. To facilitate venipuncture, the needle should be sharp, the arm extended and the vein large and fully distended.

7. The syringe must be scrupulously clean in order to prevent sticking of the plunger during injection.

8. If crystals form, the solution should be warmed and agitated until they have redissolved. Injection should be made only when the solution is clear and is at a temperature of approximately 37.5° C.

9. Injection should be made only when there is free communication between needle and vein. When in doubt, another vein should be tried or the test postponed. Vein and needle should be watched during injection to prevent displacement of the needle or overdistention of the vein. If extravasation occurs, the injection should be stopped and a quantity of physiologic saline solution administered through the needle to dilute the radiopaque medium and to lessen the possibility of irritation.

10. Some authorities advise that repeated injections should not be given in close sequence and, if possible, should be avoided.

Side Effects and Sensitivity Tests: As with other radiopaque mediums, certain side effects occasionally may be encountered, although the 75 per cent solution has been well tolerated when given in recommended dosages. Serious complications following angiocardiography may be due to varying and perhaps unrelated factors. Symptoms may be due to the speed of injection and the anxiety and psychic stress associated with the examination, as well as to the material injected. Side effects will usually be minor and transient and may include a sensation of warmth and flushing, nausea, vein cramp, mild tachycardia, metallic or acid taste, tightness in the chest, headache, cough or urticaria. Delayed reactions may occur. Venous thrombosis has not been observed in patients receiving the 75 per cent solution, but as with any rapidly injected hypertonic solution, the possibility of this complication exists.

Angiocardiographic contrast mediums may produce symptoms of an anaphylactic nature in sensitive persons. Patients should be observed carefully during injection, as serious reactions including fatalities have occurred with most mediums. Since it is believed that reactions to intravenously administered organic iodine radiopaque agents are more likely to develop in patients with allergic diathesis, special care is advisable in persons with a history of asthma or other allergic manifestations.

Various methods have been advocated to detect sensitivity to contrast mediums, particularly conjunctival, oral, intradermal and intravenous testing. Conjunctival, oral and intradermal tests are not reliable, since reactions to them are generally caused by direct local vascular effect. Occasionally a severe reaction in the eye has followed a conjunctival test. An intravenous test is more likely to demonstrate sensitivity, although a negative reaction does not necessarily rule out the possibility. A small dose of 0.5 to 1 ml. is slowly injected intravenously over a period of one minute, followed by a period of observation sufficiently long to detect delayed reactions. Although allergic reactions generally occur quickly, occasionally they may not be manifested for 10 or even 15 minutes.

Warning signs and symptoms of possible intolerance or allergy include respiratory difficulty (wheezing, dyspnea or sensation of suffocation or tightness in the throat or chest), sneezing, itching, urticaria, nausea or vomiting and fainting.
Treatment of Reactions: (Same as with Hypaque Sodium 50%)

Nephrotomography

Contraindications, Precautions, Side Effects and Treatment of Reactions: See Angiocardiography.

Hypaque®-M, 90%

brand of **sodium and meglumine diatrizoates**

Sterile Aqueous Injection 90% (weight/volume)

Caution: Hypaque-M, 90 per cent is intended primarily for angiocardiography, nephrotomography, hysterosalpingography and selected cases of peripheral angiography. Hypaque sodium

50 per cent solution is recommended for excretory urography, cerebral angiography and most cases of peripheral angiography.
Warning: Do not use Hypaque-M, 90 per cent for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

Angiocardiography

Contraindications: Use of Hypaque-M, 90 per cent is contraindicated in patients with advanced renal destruction associated with severe uremia. Hypaque-M, 90 per cent should not be used for myelography.
Precautions: 1. Caution is advised in patients with hyperthyroidism, hypertension, active tuberculosis and a history of allergy, especially to iodine. Angiocardiography and nephrotomography should be performed cautiously in patients with heart disease and circulatory failure and should not be employed in patients who are in collapse or who are critically ill or debilitated. A renal function test is advisable before administration of Hypaque-M, 90 per cent.

2. Prior to the examination, the patient may be tested for sensitivity to Hypaque-M, 90 per cent. (See Side Effects and Sensitivity Tests.) Patients who show an idiosyncrasy to Hypaque-M, 90 per cent should not be given the drug.

3. Premedication with a barbiturate is advisable if the patient is extremely nervous. Demerol (brand of meperidine), chlorpromazine and antihistamines have also been recommended for premedication. Such antihistamines as chlorpheniramine maleate or tripelennamine hydrochloride may be administered about thirty minutes before injection of Hypaque-M, 90 per cent or may be combined with it in a single injection. Many authorities recommend general anesthesia for small children and uncooperative patients.

4. Facilities for resuscitation including a mask with a breathing bag and pure oxygen should be available for immediate administration in case of severe reaction.

5. The sensations to be experienced should be described to the patient in order to allay apprehension before injection and to prevent excitement afterward.

6. To facilitate venipuncture, the needle should be sharp, the arm extended and the vein large and fully distended.

7. The syringe must be scrupulously clean in order to prevent sticking of the plunger during injection.

8. Hypaque-M, 90 per cent should be warmed and agitated until all suspended crystals have redissolved. Injection should be made only when the solution is clear and is at a temperature of approximately 37.5°C.

9. Injection should be made only when there is free communication between needle and vein. When in doubt, another vein should be tried or the test postponed. Vein and needle should be watched during injection to prevent displacement of the needle or overdistention of the vein. If extravasation occurs, the injection should be stopped and a quantity of physiologic saline solution administered through the needle to dilute the Hypaque-M, 90 per cent and to lessen the possibility of irritation.

10. Some authorities advise that repeated injections should not be given in close sequence and, if possible, should be avoided.

Hypaque®-M, 90%
brand of **sodium and meglumine diatrizoates (cont.)**

Side Effects and Sensitivity Tests: Serious complications following angiocardiography may be due to varying and perhaps unrelated factors. Symptoms may be due to the speed of injection and the anxiety and psychic stress associated with the examination, as well as to the material injected. Side effects noted with Hypaque-M, 90 per cent were usually of a minor and transient nature and included a sensation of flushing or warmth, nausea, vein cramp, mild tachycardia, metallic or acid taste, tightness in the chest, headache, cough or urticaria. Delayed reactions may occur. Venous thrombosis has been observed in patients following the percutaneous insertion of the injection needle. This complication may be anticipated, however, when concentrated hypertonic solutions are injected rapidly. In skilled hands, the administration of Hypaque-M, 90 per cent is attended by comparatively few untoward reactions.

Angiocardiographic contrast mediums may produce symptoms of an anaphylactic nature in sensitive persons. Patients should be observed carefully during injection, as serious reactions including fatalities have occurred with most mediums. Since it is believed that reactions to intravenously administered organic iodine radiopaque agents are more likely to develop in patients with allergic diathesis, special care is advisable in persons with a history of asthma or other allergic manifestations.

Various methods have been advocated to detect sensitivity to contrast mediums, particularly conjunctival, oral, intradermal and intravenous testing. Conjunctival, oral and intradermal tests are not reliable, since reactions to them are generally caused by a direct local vascular effect. Occasionally a severe reaction in the eye has followed a conjunctival test. An intravenous test is more likely to demonstrate sensitivity, although a negative reaction does not necessarily rule out the possibility. A small dose of from 0.5 to 1 ml. is slowly injected intravenously over a period of one minute, followed by a period of observation sufficiently long to detect delayed reactions. Although allergic reactions generally occur quickly, occasionally they may not be manifested for ten or even fifteen minutes.

Warning signs and symptoms of possible intolerance or allergy include respiratory difficulty (wheezing, dyspnea or sensation of suffocation or tightness in the throat or chest), sneezing, itching, urticaria, nausea or vomiting and fainting.
Treatment of Reactions: (Same as with Hypaque Sodium 50%)

Nephrotomography

Contraindications, Precautions, Side Effects and Treatment of Reactions: See Angiocardiography.

Hysterosalpingography

Contraindications: The procedure should not be performed during the menstrual period or when menstrual flow is imminent, nor should it be performed when infection is present in any portion of the genital tract, including the external genitalia. The procedure is also contraindicated for pregnant women or for those in whom pregnancy is suspected. Its use is not advised for six months after termination of pregnancy, or for thirty days after conization or curettement.
Precautions: In patients with carcinoma or in those in whom the condition is suspected, caution should be exercised to avoid possible spread of the lesion by the procedure.

Pathology Precisely Defined

Hypaque® Sodium 20% and 50%
brand of **sodium diatrizoate**

Hypaque®-M, 75% and 90%
brand of **sodium and meglumine diatrizoates**

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PSEUDOCOARCTATION OF THE AORTA ASSOCIATED WITH CONGENITAL HEART DISEASE: REPORT OF TEN CASES*

By ISRAEL STEINBERG, M.D., MARY ALLEN ENGLE, M.D., GEORGE R. HOLSWADE, M.D., *and* JACK W. C. HAGSTROM, M.D.
NEW YORK, NEW YORK

THE association of congenital heart disease with pseudocoarctation of the aorta has been previously noted.[18,20,35,39,40] Indeed, it occurred in 3 of the 16 cases reported from this center in 1962.[40] Herein are reported 10 other instances of congenital cardiac lesions associated with pseudocoarctation, with additional pathologic data from postmortem study in 2 cases. In 2 patients with persistent patent ductus arteriosus the "kink" in the aorta was obliterated following division of the ductus.

Pseudocoarctation, "kinking," or "buckling" of the arch of the aorta is uncommon; 80 cases have been previously reported.[1–3,5,6,8–13,15–35,39,40,42–45] Its recognition is important because it may be mistaken for true coarctation, aneurysm, or a mediastinal tumor. Conventional roentgenography, roentgenoscopy, and angiocardiography provide significant diagnostic data. Definitive diagnosis depends upon the demonstration of unimpeded blood flow across the area of kinking of the aorta, *i.e.*, no demonstrable pressure gradient.

REPORT OF CASES

CASE 1. *Subaortic stenosis and pseudocoarctation.* A 9 year old girl (N.Y.H. No. 877856) was discovered to have a murmur at 16 months of age, and 3 months later was seen by Dr. Helen Taussig. The murmur was thought to be due to subaortic stenosis or a ventricular septal defect. The flush blood pressure in the arm was 96, and in the leg 110 mm. Hg. Angiocardiography and countercurrent aortography disclosed a narrowing of the aorta distal to the left subclavian artery. This was interpreted as a mild coarctation.

At the age of 5 years, during one of her frequent febrile illnesses, the patient was admitted to another hospital where, in addition to the systolic murmur, a diastolic blowing murmur was heard over the aortic area. Three blood cultures had no growth. After this incident, she played actively, but tired easily.

On physical examination at the age of 9 years her height and weight were at the tenth percentile. There was a left precordial bulge and slight cardiac enlargement. A systolic thrill was felt in the suprasternal notch, over the carotid arteries, and in the second right intercostal space. A loud systolic murmur was heard maximally over the upper sternum and in the right

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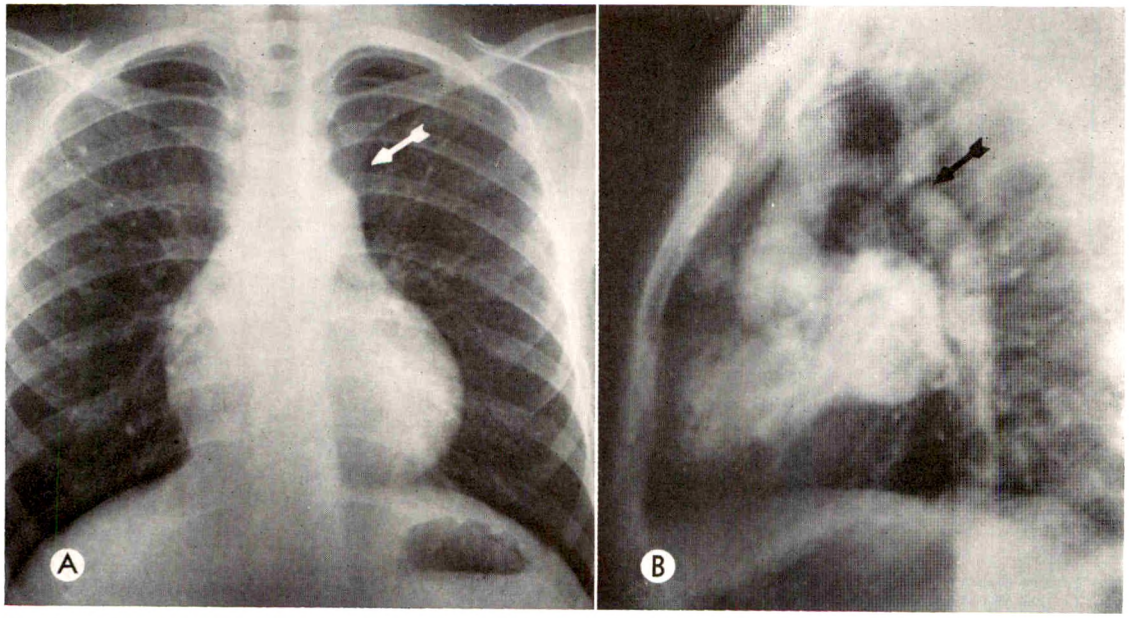


FIG. 1. Case 1. *Subaortic stenosis and pseudocoarctation.* (*A*) Frontal teleroentgenogram of the chest shows only slight enlargement of the heart and a thin vertical shadow below the left clavicle (arrow). (*B*) Lateral intravenous angiocardiogram shows deformity of the aortic root, dilatation of the ascending aorta, and kinking of the aortic arch distal to the left subclavian artery (arrow). Note absence of collateral arteries. (*B* published through the courtesy of Johns Hopkins Hospital.)

and left second intercostal spaces; it was transmitted to the neck. A soft, blowing, early diastolic murmur was detected over the second right intercostal space. The blood pressure in the arms and legs was 100/80 mm. Hg. The peripheral pulses were equal but diminished in both arms and both legs. The electrocardiogram had abnormal T waves interpreted as indicative of left ventricular "strain"; the voltage was at the upper limits of normal for the left ventricle. Phonocardiography demonstrated maximally at the upper midsternum a diamond-shaped, systolic murmur with midsystolic peak and a decrescendo diastolic murmur. Roentgenograms of the chest and roentgenoscopy showed slight cardiac enlargement and a normal aorta (Fig. 1*A*). The diagnoses were severe aortic stenosis with insufficiency and pseudocoarctation of the aorta.

The intravenous angiocardiogram, made 8 years earlier (1953), was reviewed. It showed enlargement of the left atrium and ventricle, deformity of the root of the aorta, dilatation of the ascending aorta, and indentation of the descending aorta just distal to the origin of the left subclavian artery (Fig. 1*B*).

Right and left heart catheterization performed by Dr. Daniel S. Lukas disclosed a left ventricular pressure of 203/14 mm. Hg; the simultaneous femoral artery pressure was 80/45 mm. Hg. The mean systolic gradient was 79 mm. Hg. The femoral arterial pressure tracing had a small anacrotic notch with a delayed systolic peak. Pulmonary arterial and right ventricular pressures and the cardiac output were normal. The data indicated a fixed obstruction to the left ventricular outflow tract, but the level (valvular, sub- or supravalvular) was not delineated.

At operation, a coarse systolic thrill was palpated over the root of the aorta. The pressure in the left ventricle was 200/0 mm. Hg, and in the aorta 130/85 mm. Hg. On cardiopulmonary bypass, the body temperature was reduced to 28°C. and the heart was selectively cooled further with a saline slush in the pericardial sac. The aorta was cross-clamped and a longitudinal incision was made in the root of the aorta. The aortic valve had 3 cusps and appeared normal. In the subvalvular area, however, the lumen of the outflow tract was narrowed by a fibrous ring to 3 mm. in diameter. Portions of this ring were excised and the subvalvular lumen was further dilated by use of clamps and fingers until the orifice measured 15 mm. in diameter. After the aortotomy had been closed and coronary blood

flow re-established, ventricular fibrillation was abolished by electrical counter-shock. Pressures measured before closing the chest showed abolition of the systolic gradient. The pressure in the left ventricle was 110/10 and in the aorta 110/40 mm. Hg. Her condition was satisfactory when she was taken to the recovery room, but 5 hours postoperatively cardiac arrest occurred. Efforts to resuscitate the child were unsuccessful.

Autopsy findings. The heart and lungs together weighed 450 gm. (expected weight, 353 gm.). There was quadrichamber enlargement with selective hypertrophy of the right and left ventricles, the walls of which were 4 and 13 mm. thick respectively. A few old interstitial scars were present in multiple sections of the myocardium and papillary muscles of both ventricles. The endocardial surface of the distal portion of the left ventricular outflow tract was thickened up to 2 mm. by a circumferential band of dense, white, fragmented tissue that was about 7 mm. in width and that extended onto and thickened the 3 cusps of the aortic valve. The circumference of the outflow tract, where the endocardium was thickened, was 2.9 cm. Although much of this dense tissue had been surgically removed, the remainder could be easily peeled off. After peeling this tissue off the cusps of the aortic valve, they were diaphanous and in every other way normal. The endocardium of the outflow tract underlying this tissue, after peeling, was normal grossly. The sinuses of Valsalva were unusually deep prior to removal of the abnormal tissue, but were normal after removal. The coronary arteries were normal.

Microscopically the line of cleavage that was so evident in the gross specimen was equally clear. The accumulated tissue was composed of bundles of tangled filaments that stained as collagen. The main mass of the tissue was hypocellular and contained only a few fibrocytes and primitive mesenchymal cells. In areas where it had been surgically disrupted, there were deposits of material that stained positively with the Lendrum stain for fibrin. In undisturbed areas the mass of tissue was covered by endothelium. This tissue that formed the subaortic ring was entirely superficial and did not in any area invaginate into the myocardium. The endocardium of the outflow tract of the right ventricle was also thickened, but much less and more diffusely. There the collagen fibers did extend into and interdigitated with myofibers in the inner one-third of the underlying myocardium.

A 2 cm. long longitudinal incision in the root of the aorta was closed by silk sutures. The circumferences of the aorta were as follows: at the root, 4 cm.; just proximal to the innominate artery, 3.5 cm.; 2 cm. distal to the left subclavian artery, 3.0 cm. At the insertion of the ligamentum arteriosum 2 narrow ridges projected into the lumen no more than 1 mm. Sections through this area showed that the obliterated ductus arteriosus approached the adventitial surface of the aorta perpendicularly and then it ran parallel with the aorta for a distance of about 3 mm. The obliterated aortic ostium of the ductus arteriosus was between the 2 intimal projections. The media of the aorta immediately proximal and distal to the ligamentum arteriosum was thickened by elastic fibers that coarsed in several directions. All other sections of the aorta were normal. The 2 projections into the lumen were composed of proliferated collagen fibers (intima) and contained no elastic fibers. These ridges presumably originated as a result of the protracted tension on the aorta by the ligamentum arteriosum as it paralled the course of the aorta. It is at this point that the kink in the aorta occurred.

Sections of the lungs had changes indicative of chronic passive congestion and preterminal aspiration of gastric contents.

The final anatomic diagnoses were: subaortic stenosis, pseudocoarctation of the aorta, and aspiration of gastric contents.

Case II. *Coarctation of aorta converted to pseudocoarctation by division of silent patent ductus arteriosus*. A 14 year old boy (N.Y.H. No. 809189) was admitted to The New York Hospital because of a cardiac murmur first detected at the age of 7 years. His height and weight were near the 50th percentile. A harsh systolic murmur was heard maximally over the second and third left interspaces and radiated into the neck. It was especially well heard in the left interscapular area at the level of the third thoracic vertebra. The heart sounds were normal. Wrist pulses were normally full, but the pulses in the legs were diminished. Blood pressures were as follows: right arm, 140/60; left arm 125/60; right and left legs 110/85 mm. Hg. Oscillometric readings disclosed faint pulsations in the legs, lagging in comparison to those in the

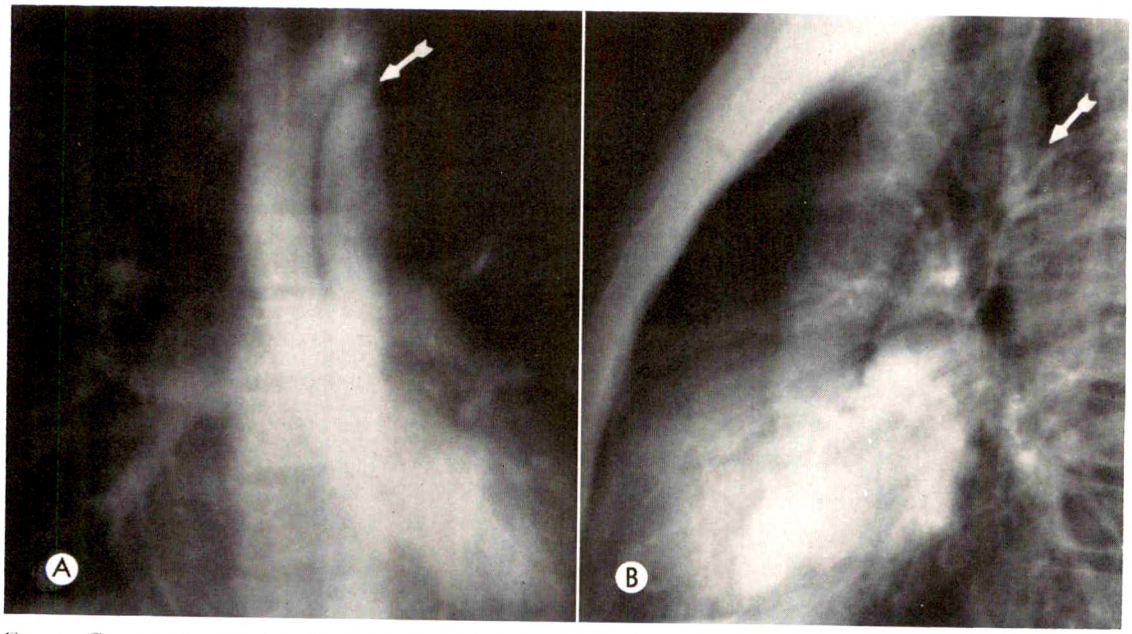


FIG. 2. Case II. *Coarctation of aorta converted to pseudocoarctation by division of silent ductus arteriosus.* (*A*) Frontal intravenous angiocardiogram shows deformity of the aortic arch (arrow) just beyond the origin of the left subclavian artery. Note the absence of collateral circulation. (*B*) Left anterior-oblique intravenous angiocardiogram better demonstrates the kinked aorta (arrow), dilatation of the descending aorta, and absence of arterial collaterals.

arms. The electrocardiogram showed incomplete right bundle branch block but no changes associated with ventricular hypertrophy. A normal cardiac silhouette without notching of the ribs was present in a roentgenogram of the chest. Frontal and lateral views of the intravenous angiocardiograms disclosed a deformity of the aorta, but increased arterial collaterals were absent (Fig. 2, *A* and *B*). The diagnosis was mild coarctation of aorta.

An operation was performed under hypothermia of 31.4°C., employed because of the absence of significant collateral circulation, to decrease the possibility of spinal cord damage should prolonged cross-clamping of the aorta be necessary. One and one-half cm. distal to the left subclavian artery, the external diameter of the aorta was narrowed. A short, funnel-shaped patent ductus arteriosus, 4 mm. in diameter, joined the aorta just distal to this point. Moreover, the aorta was kinked at the point of insertion of the ductus owing to the medial traction it exerted. After division and closure of the ends of the ductus, not only was the traction and angulation decreased, but the coarctation was less apparent externally. Aortic pressure proximal to the area of narrowing was 145/95 and distal to this point it was 130/95 mm. Hg, giving a peak systolic gradient of only 15 mm. Hg. Since a small internal diaphragm was suspected, the aorta was cross-clamped above and below and opened transversely at the point of narrowing. A ridge, 1–3 mm. in width, partially encircled the aorta at this point. This ridge was trimmed off of the luminal surface. After the aortic clamps were released, pressures recorded again were unchanged. To overcome this small gradient it would have been necessary to resect a segment of aorta 3 cm. in length and to insert a graft; this was not thought to be advisable. The postoperative course was uncomplicated.

Six years later, when the patient was readmitted because of infectious mononucleosis, the electrocardiogram was unchanged. A soft systolic murmur was still heard with maximal intensity in the second left intercostal interspace and posteriorly in the left interscapular area. The peripheral pulses were normal in volume and timing in all extremities. The blood pressure was now equal in the arms and in the legs at 120/80 mm. Hg.

CASE III. *Coarctation converted to pseudocoarctation by division of small silent patent ductus*

arteriosus. A 20 year old man (N.Y.H. No. 974358) was referred to The New York Hospital because of hypertension and easy fatiguability of 2 years' duration. A heart murmur had been heard from the age of 3. He was 184 cm. tall and weighed 77 kg. The blood pressure in the arms was 180/90 and in the legs 125/90 mm. Hg. Femoral and pedal arterial pulses were palpable but were delayed and weaker than those in the radial and carotid arteries. A systolic ejection-type murmur was heard over the base of the heart; it radiated into the neck arteries. A similar murmur was also heard posteriorly over the second to third thoracic vertebrae. The heart sounds were normal, and there was no diastolic murmur. A phonocardiogram substantiated these findings. Regular sinus rhythm, incomplete right bundle branch block, and no evidence of ventricular hypertrophy were noted on the electrocardiogram. Slight prominence of the left ventricle and subclavian artery were seen on a roentgenogram of the chest. The diagnosis was coarctation of the aorta. Supravalvular aortography (Fig. 3, *A-C*) revealed a deformity of the arch of the aorta 3 cm. distal to the left subclavian artery and no increase in collateral arterial supply. There was no evidence of patency of the ductus arteriosus (Fig. 3, *A-C*) by aortography or auscultation.

Owing to the absence of collateral circulation, provisions were made at operation for a left-atrial-to-femoral-arterial bypass should prolonged cross-clamping of the aorta be necessary. A small patent ductus arteriosus, 3 mm. in diameter and 8 mm. in length, pulled the aorta anteriorly and superiorly, causing a kink at the point of insertion. There was apparent fusiform narrowing of the aorta for a distance of 2 cm. at the level of the insertion of the ductus. After the ductus was divided, the aorta straightened out. Pressures were recorded from several sites above and below the area of relative narrowing and all were found to be 120/80 mm. Hg. Neither ridge nor diaphragm was palpable within the lumen of the aorta, so it was elected not to open the aorta. At discharge on the ninth postoperative day, the pressure was 150/80 in the upper extremity and 120/80 mm. Hg in the lower extremity. By 3 months later, the pressure in the upper extremity was 150/90 and in the lower extremity, 140/90 mm. Hg. Six months after surgery, the blood pressure in the

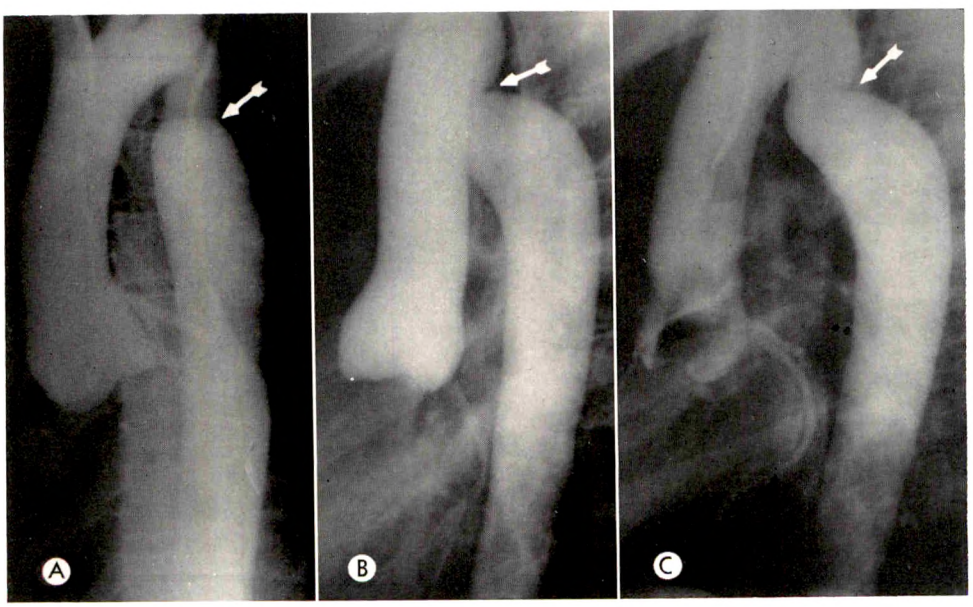


Fig. 3. Case III. *Coarctation of aorta converted to pseudocoarctation by division of silent small patent ductus arteriosus*. (*A*) Frontal (slightly oblique) selective aortogram shows narrowing of the aortic arch just beyond the left subclavian artery (arrow), poststenotic dilatation of the descending aorta, and absence of collateral arteries. (*B*) Lateral aortogram, biplane view of (*A*), also shows the kinking of the aortic arch (arrow), poststenotic dilatation, and absence of collateral arterial circulation. (*C*) Left anterior oblique selective aortogram demonstrates to advantage the deformed aortic arch (arrow) and poststenotic dilatation of the descending aorta.

upper and lower extremities was equal at 140–145/80–90 mm. Hg.

CASE IV. *Pseudocoarctation, small ventricular septal defect, aortic valvular stenosis, and anomalous common origin of innominate and carotid arteries.* A 7 year old girl (N.Y.H. No. 929383) at the time of right and left heart catheterization and contrast cardiovascular visualization studies, had been noted at 1 month to have a holosystolic murmur. A month later 4 chamber cardiac enlargement was seen on a roentgenogram of the chest. The main pulmonary artery was dilated and the pulmonary vascular markings were increased. Changes in the electrocardiogram indicated marked left and moderate right ventricular hypertrophy. The clinical impression was a ventricular septal defect with early cardiac decompensation. She was given digitalis and responded well.

At 11 months of age, an ejection-type murmur was heard. The heart was still enlarged, but the pulmonary vascular markings were less prominent. At this time a left ventricular anomaly, perhaps subaortic stenosis with or without endocardial fibroelastosis was considered; the earlier impression of ventricular septal defect was questioned. Six months later, roentgenography showed the heart size to be at the upper limits of normal, and a year later, it was normal.

The patient was first seen at this hospital at the age of 3 years. Physical examination revealed the blood pressure to be 110/70 in the arms and 120/70 mm. Hg in the legs. There was a slight left parasternal bulge with a faint systolic thrill in the fourth left interspace; there was no cardiomegaly. A high-pitched pansystolic murmur, heard maximally along the lower left sternal border, was transmitted to the apex and posteriorly to the lung fields. A rougher, ejection-type, systolic murmur was heard over the base of the heart on the right; it was transmitted to the neck. The second sound was normal. Diastole was clear except for a third heart sound. A phonocardiogram recorded a plateau-shaped, holosystolic murmur over the fourth left interspace, and over the second right interspace, a diamond-shaped systolic murmur with early systolic ejection sound. The electrocardiographic changes were diagnosed as incomplete right bundle branch block and left ventricular hypertrophy. Roentgenograms of the chest and cardiac roentgenoscopy showed only slight enlargement of the left ventricle (Fig. 4, *A* and *B*).

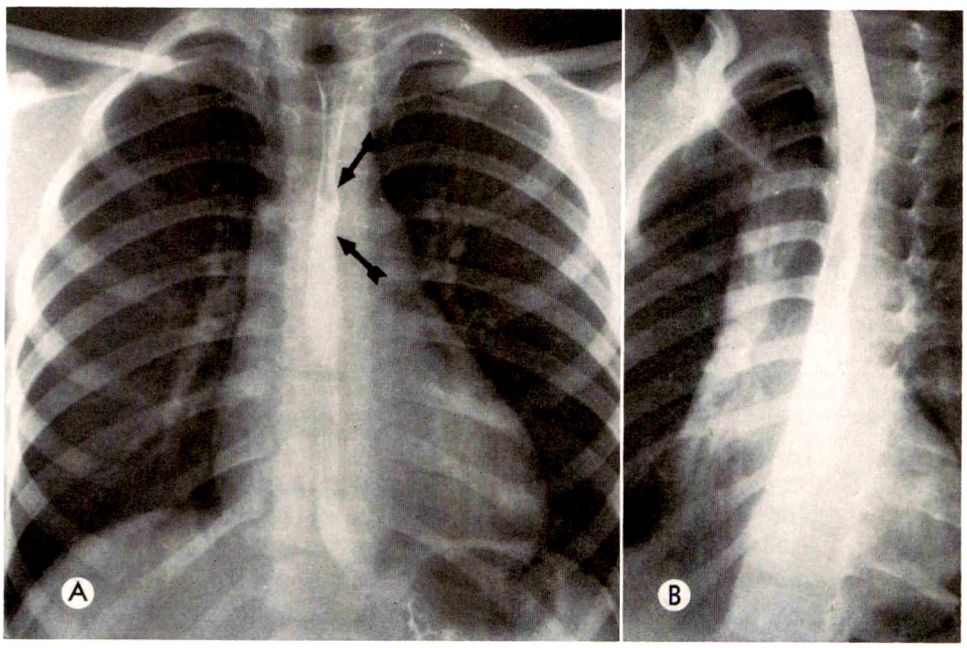


FIG. 4. Case IV. *Pseudocoarctation, small ventricular septal defects, aortic valvular stenosis, and anomalous common origin of innominate and carotid arteries.* (*A*) Frontal roentgenogram shows slight enlargement of the left ventricle and the reversed figure "3" deformity of the esophagus owing to the double aortic shadows (arrows). (*B*) Left anterior oblique roentgenogram shows better the enlargement of the left ventricle as well as the "E" sign in the esophagogram and the "3" sign in the descending aorta.

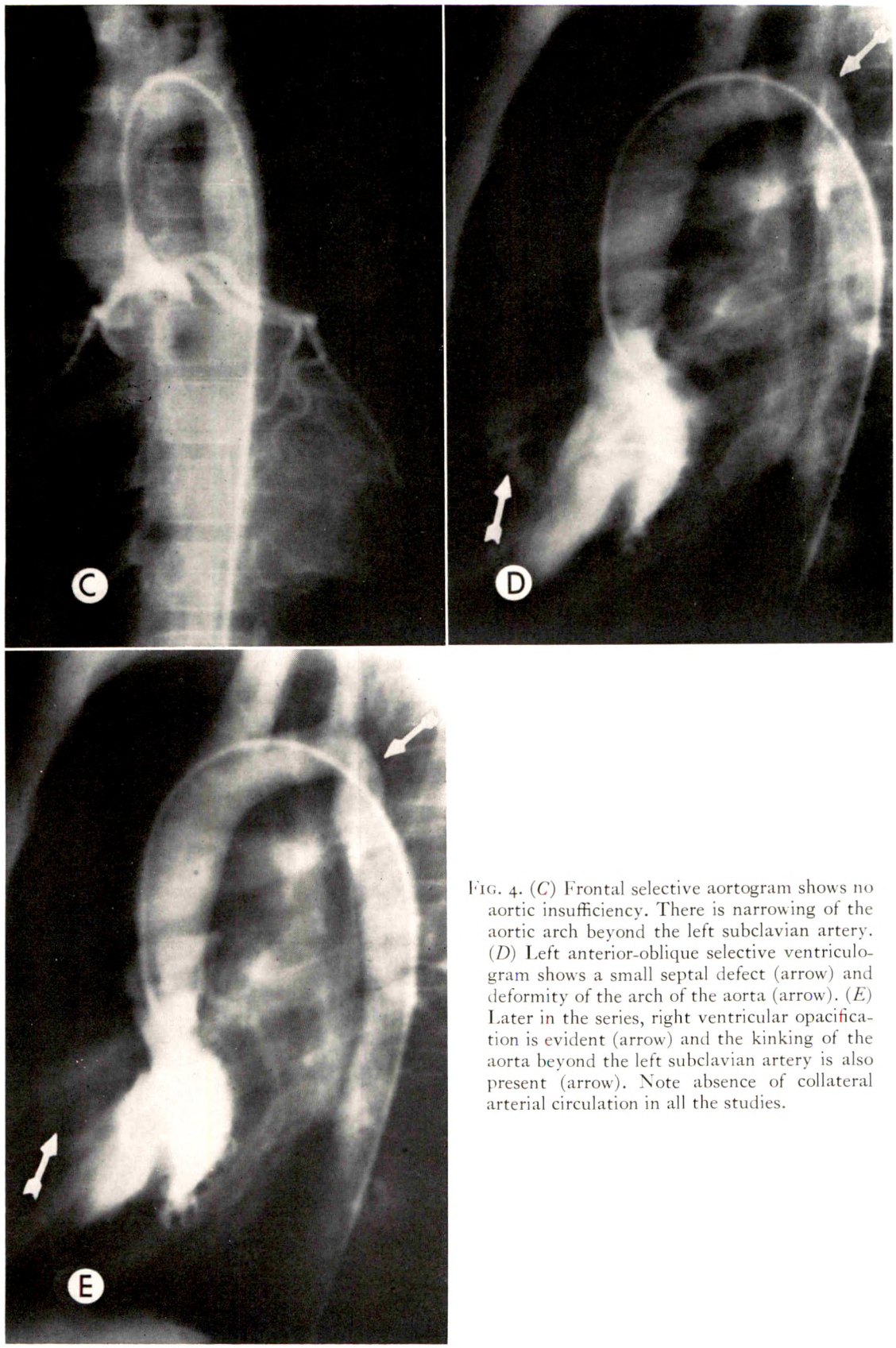


FIG. 4. (*C*) Frontal selective aortogram shows no aortic insufficiency. There is narrowing of the aortic arch beyond the left subclavian artery. (*D*) Left anterior-oblique selective ventriculogram shows a small septal defect (arrow) and deformity of the arch of the aorta (arrow). (*E*) Later in the series, right ventricular opacification is evident (arrow) and the kinking of the aorta beyond the left subclavian artery is also present (arrow). Note absence of collateral arterial circulation in all the studies.

A deformity of the barium-filled esophagus in frontal (Fig. 4*A*) and left anterior oblique (Fig. 4*B*) views showed changes such as are seen with coarctation of the aorta (the "E" sign). The adjacent descending aorta, seen in profile in the left anterior oblique projection, appeared to first narrow and then widen, the "3" sign associated with coarctation of the aorta. The main pulmonary artery and pulmonary vascular markings were normal.

The patient remained asymptomatic after discontinuation of digitalis at the age of 4 years and when she was admitted at the age of 7 years to confirm the diagnoses of a small ventricular septal defect and aortic stenosis. On selective angiocardiography the ascending aorta was moderately dilated and there was common origin of the left common carotid and innominate arteries from the arch. The coronary arteries were normal. Left ventricular injection of contrast medium confirmed the suspicion of mild aortic valvular stenosis, opacified 2 muscular ventricular septal defects, and showed the left ventricle to be somewhat hypertrophied. There was a definite pseudocoarctation (Fig. 4, *C-E*).

CASE V. *Pseudocoarctation with atrial septal defect and aortic stenosis (both surgically corrected)*. A 45 year old man (N.Y.H. No. 878717) was readmitted because of dyspnea of 8 weeks' duration. Six years earlier he had had an atrial septal defect repaired in this hospital and was well until dyspnea developed on climbing a flight of stairs. He had no chest pain but he was easily fatigued. Examination revealed a well developed, robust man. The point of maximum impulse of the heart was beyond the left midclavicular line in the fifth intercostal space. An ejection-type systolic murmur, without radiation to the neck, was heard over the base of the heart. S2 was unduly split and there were no diastolic murmurs. The blood pressure in the arms was 138/80 mm. Hg, and in the legs it was also normal. The electrocardiograms showed evidence of incomplete atrioventricular block, marked left axis deviation, and ST and T wave abnormalities probably due to digitalis.

In roentgenograms of the chest (Fig. 5*A*) there was enlargement of the left ventricle, slight deformity of the arch of the aorta, and a calcified aortic valve. Selective retrograde aortography disclosed a severely stenosed, bicuspid aortic valve with an 80 mm. Hg peak systolic and a 53 mm. mean systolic gradient across the valve, mild aortic insufficiency, dilatation of the aortic sinuses, and pseudocoarctation of the thoracic aorta (Fig. 5, *B* and *C*). Data from cardiac catheterization performed by Dr. Daniel S. Lukas, showed the following: a small left-to-right shunt at the atrial level; a mean systolic pressure gradient of 53 mm. Hg between the left ventricle and aorta; elevation of the left ventricular pressure to 181/20 mm. Hg; and calculated stenosis of the aortic orifice of 0.7 mm.[2] The left-to-right shunt at the atrial level was confirmed by hydrogen and ascorbate dilution tests.

An open-heart procedure was performed via a median sternotomy incision through which the area of the pseudocoarctation of the thoracic aorta could not be visualized. Pressures were recorded as follows: left ventricle, 220/25; aortic root, 128/68; and femoral artery 125/65 mm. Hg. A heavily calcified, bicuspid aortic valve was excised and replaced with a No. 9 Starr-Edwards artificial prosthesis. A 3×5 mm. residual atrial septal defect was closed. Pressures after cardiopulmonary bypass revealed a 2 mm. peak systolic gradient across the artificial aortic valve.

Five days after the operation the sternotomy incision dehisced; microorganisms of the *Klebsiella-Aerobacter* group were cultured from the sternum. Colistin was added to the methicillin he had received since surgery, but he continued to have an elevated temperature (38–39°C.) and an anemia for 1 month. After the fever disappeared, he was discharged, only to be readmitted a week later because the fever reoccurred. Blood cultures were obtained, and antibiotic therapy was begun when a diphtheroid organism was recovered. The heart was moderately enlarged and a loud murmur and a ball click were heard along the upper sternal border. After a few days, a faint early diastolic murmur of aortic insufficiency appeared. Roentgenograms of the chest on admission showed that the heart was enlarged. Ten days later, the position of the prosthesis had changed, and cinefluoroscopy revealed a rocking motion of the valve. Aortography showed a moderate reflux of contrast material into the left ventricle and a lobulated aneurysm of the left aortic sinus of Valsalva. Because of these findings and the development of cardiac failure, the patient was reoperated upon. The prosthesis rocked easily in its setting, which was infected. The valve ring and root of the aorta were friable and the

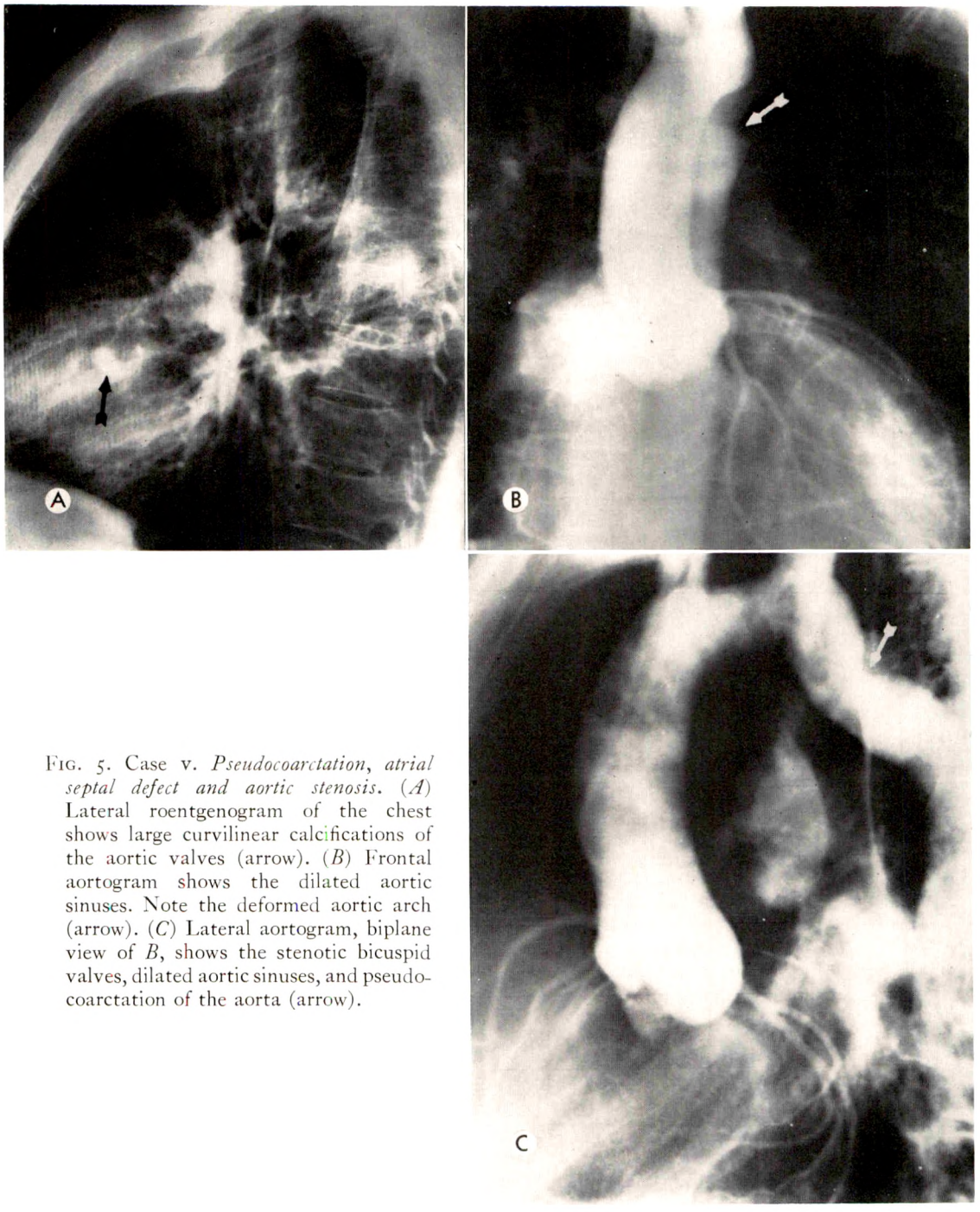


Fig. 5. Case v. *Pseudocoarctation, atrial septal defect and aortic stenosis.* (*A*) Lateral roentgenogram of the chest shows large curvilinear calcifications of the aortic valves (arrow). (*B*) Frontal aortogram shows the dilated aortic sinuses. Note the deformed aortic arch (arrow). (*C*) Lateral aortogram, biplane view of *B*, shows the stenotic bicuspid valves, dilated aortic sinuses, and pseudocoarctation of the aorta (arrow).

left aortic sinus of Valsalva was irregularly dilated. Cultures of the necrotic material around the prosthesis and of the pericardial fluid subsequently grew microorganisms of the *Klebsiella-Aerobacter* group. The old prosthesis was replaced and the area of the valve ring debrided. Despite respiratory and cardiac assistance, the patient died in the recovery room.

Autopsy. Postmortem examination confirmed the presence of infection in the area of the aortic valve ring and root of the aorta. They were necrotic and heavily infiltrated by neutrophils

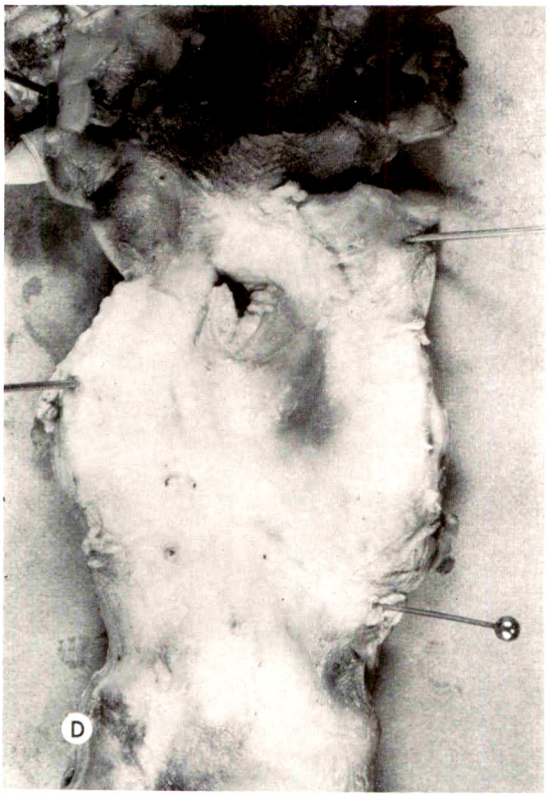


FIG. 5. (*D*) Gross specimen of aorta at the level of the pseudocoarctation shows the deformity of the aortic wall and the dimple of the obliterated ductus arteriosus.

and chronic inflammatory cells. The atrial septal defect was closed. The area of pseudocoarctation of the aorta was identified as an infolding without a diaphragm at the level of the dimple of the ligamentum arteriosum (Fig. 5*D*). Microscopically this area did not differ from the adjacent aorta. There was moderate atherosclerosis.

The final anatomic diagnoses were: atrial septal defect and aortic stenosis in a bicuspid valve, both surgically repaired; pseudocoarctation of the aorta; and bacterial endocarditis.

CASE VI. *Double pseudocoarctation (pre- and post left subclavian artery) and aneurysm of the right aortic sinus of Valsalva.* The patient (N.Y.H. No. 938388) was referred for cardiac evaluation at the age of 6 months. An incomplete cleft palate, micrognathia, bilateral hammer-toe deformity of the fourth toe, and a cardiac murmur were noted in the newborn nursery, but the neonatal period was uncomplicated. The left precordium was full and the heart was slightly enlarged. A harsh thrill was palpated in the suprasternal notch, second right interspace, and over the precordium. An ejection-type systolic murmur with an early systolic ejection sound was maximal over the left sternal border and was well heard over the second right interspace, upper sternum, and suprasternal notch. The murmur radiated throughout the precordium, into the neck arteries, and throughout the lung fields. S2 was physiologically split and both components were of average intensity. A short, late, diastolic murmur was audible at the apex. Pulsations in the femoral arteries were less strong than in the radial arteries. Blood pressure was 120/80 mm. Hg in the arms and could not be well heard in the popliteal spaces.

Some left ventricular enlargement, but no enlargement of the left atrium or right side of the heart, was observed on roentgenography and roentgenoscopy. The main pulmonary artery was normally convex and the pulmonary vascular markings were average. Barium swallow delineated a left aortic arch and descending aorta without left atrial enlargement. An indentation in the aorta at the usual level of a coarctation was present in the left anterior oblique projection. Changes in the electrocardiogram indicated right bundle branch block and left ventricular hypertrophy. The clinical impression was that she had aortic stenosis and coarctation of the aorta.

At 23 months of age, she was admitted for repair of the cleft palate and was prophylactically given therapeutic doses of penicillin for 3 days. At that time, the pulsations in the femoral arteries were equal to those in the arms. From the age of $3\frac{1}{2}$ years the blood pressures in the arms and legs were the same or with at most a 10 mm. difference. She continued to be asymptomatic and to have normal growth and development.

At the age of 4 years, she was admitted for cardiac catheterization and contrast visualization studies. Her physical and laboratory findings were unchanged from the initial ones. At catheterization, there was no left-to-right nor right-to-left shunt, and pressures in the right side of the heart were normal. The left ventricle could not be entered in a retrograde fashion, nor could it be entered via a patent foramen ovale from the right atrium. Injection of contrast medium into the main pulmonary artery

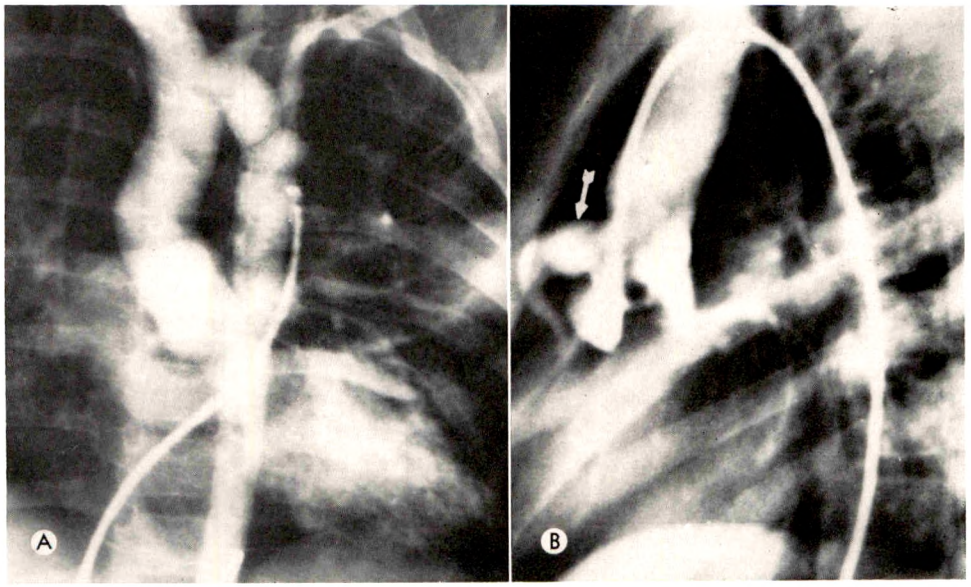


Fig. 6. Case vi. *Double pseudocoarctation and aneurysm of right aortic sinus of Valsalva.* (*A*) Frontal aortogram shows double aortic narrowing. (*B*) Selective aortogram shows the right aortic sinus aneurysm (arrow) and aneurysmal orifice of the right coronary artery.

revealed normal pulmonary arterial and venous patterns. The aortic valve was deformed and narrowed, and the right aortic sinus of Valsalva was aneurysmally dilated (Fig. 6*B*). Two areas of narrowing were observed in the descending aorta, one was just proximal to and the other distal to the left subclavian artery (Fig. 6*A*). There was a trivial pressure gradient between the ascending and descending aorta with a peak systolic pressure gradient of 6 mm., and a mean systolic gradient of 3 mm. Hg. The pressure in the ascending aorta was 96/58, with a mean of 78, and in the descending aorta it was 90/60, with a mean of 75 mm. Hg. At the end of these studies the diagnosis was changed to pseudocoarctations of the aorta with aneurysm of the sinus of Valsalva at the point of origin of the dilated right coronary artery in addition to aortic valvular stenosis.

Case vii. *Pseudocoarctation and aneurysm of left subclavian artery.* An asymptomatic 58 year old man was referred by Dr. A. Lee Winston for angiocardiography because of an unusual chest roentgenogram (Fig. 7*A*). Pressures were normal in arms and legs. Angiocardiography in biplane, frontal and lateral views showed normal cardiac chambers and pulmonary circulation. The ascending aorta was of normal caliber but there was a kink of the transverse aorta and narrowing just beyond the left subclavian artery. The left subclavian artery was markedly dilated. The descending aorta was of normal caliber (Fig. 7, *B* and *C*). The diagnosis was pseudocoarctation of the arch of the aorta with aneurysmal dilatation of the left subclavian artery.

Case viii. *Pseudocoarctation of the aorta and large ventricular septal defect.* A 4 month old baby girl (N.Y.H. No. 1044127) was hospitalized here in congestive cardiac failure. She exhibited respiratory distress though no cyanosis and she had an enlarged, overly active heart with bulging precordium; a holosystolic thrill and murmur maximal over the lower sternal border; an accentuated, single S2 in the second left interspace; and a mid-diastolic murmur at the apex. Peripheral pulses were normal in all extremities. Blood pressure was 90/65 in the arms and 95/65 in the legs. Cardiac series of roentgenograms showed a markedly enlarged heart involving all 4 chambers but especially the left atrium and ventricle, and a convex pulmonary artery with greatly increased vascular markings (Fig. 8, *A* and *B*). Electrocardiogram indicated hypertrophy of the left atrium and ventricle. Phonocardiogram recorded the auscultatory findings.

After intensive medical management of the cardiac failure resulted in improvement, she underwent cardiac diagnostic studies. Cardiac

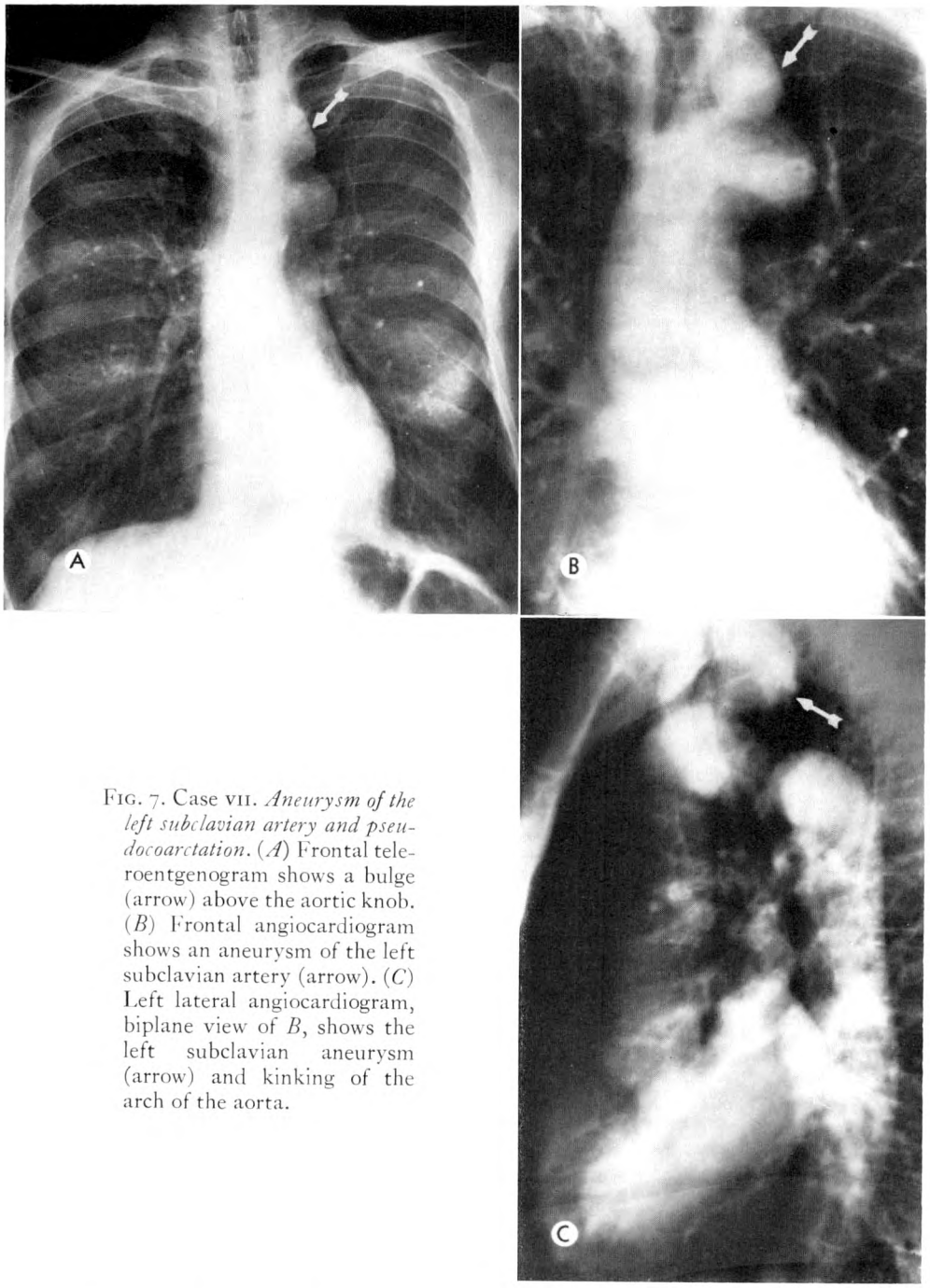


FIG. 7. Case VII. *Aneurysm of the left subclavian artery and pseudocoarctation.* (*A*) Frontal teleroentgenogram shows a bulge (arrow) above the aortic knob. (*B*) Frontal angiocardiogram shows an aneurysm of the left subclavian artery (arrow). (*C*) Left lateral angiocardiogram, biplane view of *B*, shows the left subclavian aneurysm (arrow) and kinking of the arch of the aorta.

catheterization by Dr. Daniel S. Lukas confirmed the diagnosis of large ventricular septal defect with pulmonary hypertension. The pressure in the pulmonary artery was 92/49 while that in the aorta was 94/42 mm. Hg. There was a bidirectional shunt at the ventricular level. The catheter entered the aorta from the right ventricle. Selective aortography disclosed the unsuspected presence of 4 areas of kinking or pseudocoarctation without a pressure gradient. One was just beyond the origin of the left common carotid artery, and the other was 2 cm. below the left subclavian artery. No vessels of collateral circulation were seen. There was di-

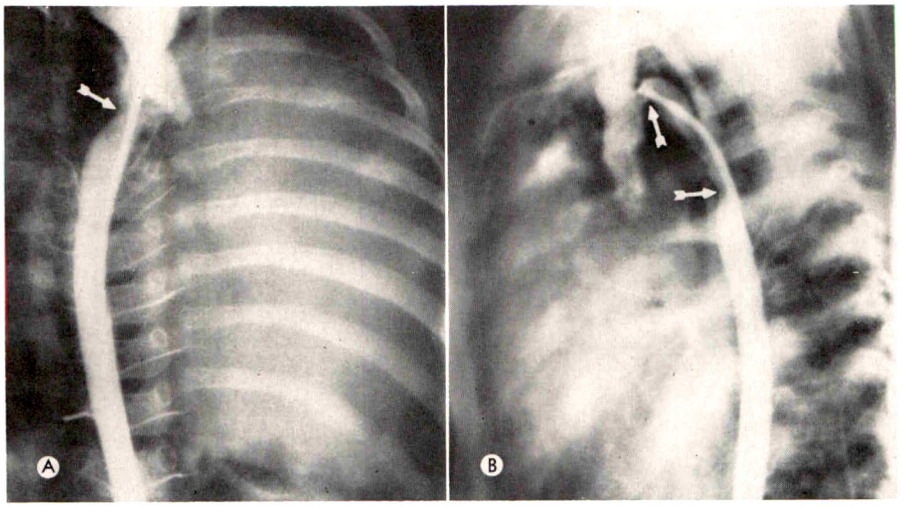


Fig. 8. Case VIII. *Pseudocoarctations of the aorta and large ventricular septal defect.* Selective retrograde aortogram with catheter introduced from femoral artery in biplane frontal (*A*) and lateral (*B*) views shows two areas of narrowing of the aorta (arrows). The first is seen in the lateral view (*B*) near the tip of the catheter just distal to the left common carotid artery. The aorta is dilated just distal to this narrowing and then is constricted again below the level of the left subclavian artery at the level of a usual true coarctation. There is postconstrictive dilatation of the aorta below this second area also (*A* and *B*). In frontal view (*A*) the descending aorta swings widely to the right as it descends in the thorax. This lateral displacement is probably due to the left atrial enlargement.

latation of the aorta just distal to each of these kinks. Although the aorta arched to the left, it deviated to the right as it descended in the thorax. The possibilities of origin of both great arteries from the right ventricle or of single ventricle were not excluded by these studies, since a left ventricular injection could not be made. However, this was accomplished at the age of $2\frac{1}{2}$ years by Dr. Aaron Levin. Again she had a systemic pressure in the pulmonary artery with a greater left-to-right than right-to-left shunt. Selective left ventricular angiocardiogram confirmed the large ventricular septal defect and demonstrated normal origin of the great arteries. The 2 areas of slight narrowing in the arch of the aorta were unchanged. She has continued on digitalis and is a candidate for closure of the septal defect.

Case IX. *Pseudocoarctation of aorta, single ventricle, D-transposition of the great arteries, and valvular pulmonic stenosis.* An 8 year old boy (N.Y.H. No. 851524) has been under regular pediatric cardiac follow-up at this hospital since birth because of cyanosis. The second sound in the second left interspace was single. No murmur was heard over the precordium but a soft systolic murmur was audible posteriorly over the lung fields. At 8 months of age a systolic murmur was audible over the lower precordium. Peripheral pulses were normal in the arms and legs. On roentgenograms, the heart was average sized and boot shaped. The pulmonary arterial markings were diminished. His electrocardiogram since birth showed extreme right axis deviation and right ventricular hypertrophy. At 15 months of age polycythemia began progressively to increase. By the age of 2 years he still could not walk. He was admitted then for a Blalock-Taussig anastomosis with the impression that he had a variant of a tetralogy of Fallot. After the end of the left subclavian artery was anastomosed to the side of the left pulmonary artery, a continuous murmur of a functioning anastomosis appeared. He became increasingly active and his polycythemia decreased from a hematocrit of 69.5 per cent and a hemoglobin of 23.5 gm. per cent preoperatively to a hematocrit of 58 per cent and hemoglobin of 18 gm. per cent postoperatively.

At the age of 5 years he was readmitted for cardiac diagnostic studies. His height and weight were at the 90th percentile for his age, as they had been since his operation. He had slight cyanosis at rest with moderate clubbing. An ejection-type systolic murmur was audible over the base of the heart anteriorly. The second sound was single in the second left interspace. A

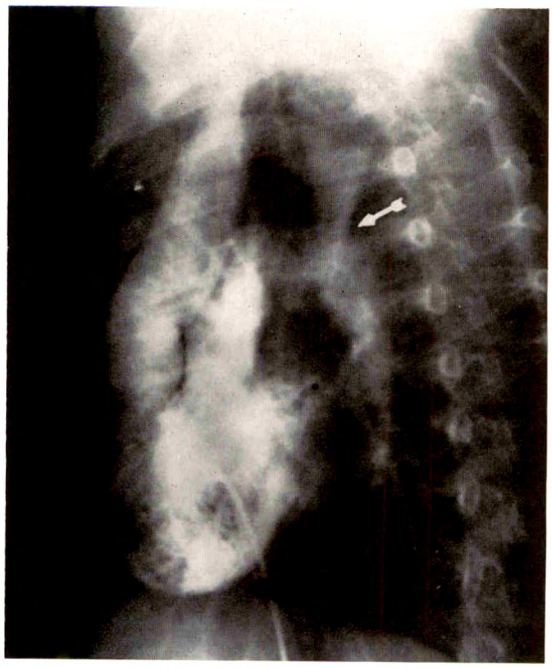


FIG. 9. Case IX. *Single ventricle, D-transposition of great arteries, pulmonic stenosis, and pseudocoarctation.* Left lateral view following injection of contrast medium into the single ventricle shows the aorta anterior to the pulmonary artery. The ascent of the aorta is unusually elongated, and there is a kink in the descending aorta distal to the left subclavian artery (arrow). The pulmonic valve in several roentgenograms appeared domed and thickened.

faint continuous murmur was heard over the posterior left chest. Blood pressure was 90/70 in the arms and 100/70 mm. Hg in the leg, and the femoral and brachial arterial pulses were of equal volume. Electrocardiogram continued the same. The cardiac series of chest roentgenograms showed an average sized boot shaped heart with average pulmonary vascularity. Selective angiocardiograms with injection into the ventricle, which the catheter entered from the right atrium by way of the inferior vena cava, indicated that there was a common ventricle with the aorta anterior to the pulmonary artery. The pulmonic valves were thickened and had a domed appearance during systole suggesting valvular pulmonic stenosis. The catheter could not be maneuvered into the main pulmonary artery. The left subclavian artery was patent at the anastomosis. An area of narrowing of the aorta distal to the left subclavian artery was well seen (Fig. 9). No pressure gradient was measured across this area of pseudocoarctation.

The impression following these studies was that he had a single ventricle with D-transposition of the great arteries, valvular pulmonic stenosis and a functioning subclavian-pulmonary arterial anastomosis.

CASE X. *Pseudocoarctation with probable congenital heart disease (suspected ventricular septal defect).* This 55 year old asymptomatic woman was studied by Dr. Gary E. Swanson of Calgary, Canada on July 13, 1967, because of the finding of a mediastinal mass on a routine roentgenogram of the chest (Fig. 10*A*). The right arm blood pressure was 100/70, the left arm 98/70, and the right leg was 90/68 mm. Hg. A pansystolic murmur (Grade 3–4) was heard over the lower midprecordium. Selective retrograde aortography via the right femoral route disclosed a dilated descending aorta with a kink (Fig. 10, *B* and *C*). Cardiac catheterization has not been performed; so the small ventricular septal defect, suspected from the location and holosystolic timing of the murmur, has not been fully evaluated.

DISCUSSION

In 1951, Dotter and Steinberg[12] in their report on anomalies of the arch of the aorta described 2 patients with what we now call pseudocoarctation and commented on its resemblance to true coarctation. In the same year, Robb[28] reported a case while Souders *et al.*[33] published data on 3 patients who initially were thought to have mediastinal tumors but were later diagnosed as having subclinical coarctation. In 1952, Dotter and Steinberg[13] reported another case and again proposed that this deformity be called pseudocoarctation. In 1955, DiGuglielmo and Guttadauro[11] described 2 patients with a similar aortic arch deformity which they called "kinking" of the aorta. In 1956, again from this Center,[35] a patient was described with dilatation of the aorta, aneurysmal dilatation of the aortic sinuses, and deformity of the arch of the aorta (pseudocoarctation) without an aortic pressure gradient. Shortly thereafter, Bruwer and Burchell,[9] Vaughan,[45] and Bruwer[10] also reported cases of anomalies of the

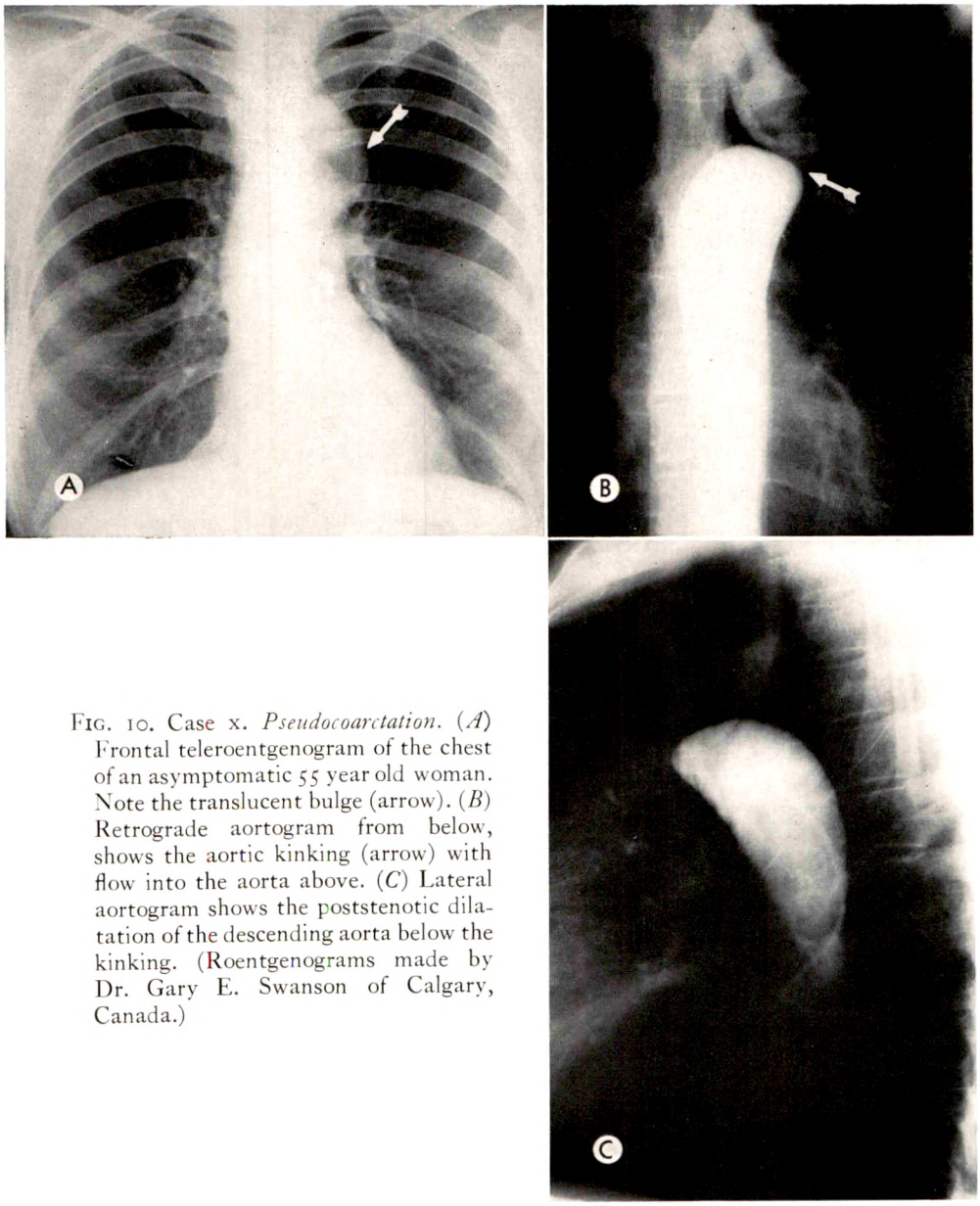


Fig. 10. Case x. *Pseudocoarctation.* (*A*) Frontal teleroentgenogram of the chest of an asymptomatic 55 year old woman. Note the translucent bulge (arrow). (*B*) Retrograde aortogram from below, shows the aortic kinking (arrow) with flow into the aorta above. (*C*) Lateral aortogram shows the poststenotic dilatation of the descending aorta below the kinking. (Roentgenograms made by Dr. Gary E. Swanson of Calgary, Canada.)

arch of the aorta, referred to as "kinking" of the arch of the aorta. In 1957, Samuel and Morris[30] reported 2 patients. In 1958, Stevens[43] in contributing 4 new cases of anomalies of the arch of the aorta suggested that the lesions be called "buckling" of the arch of the aorta. Pattinson and Grainger,[25] in 1959, added 5 cases under the title of "congenital kinking of the aortic arch." Barrett and Verney[3] recently called attention in their 2 cases to fusiform aneurysmal dilatation of the descending aorta. In the cases studied by Edmunds *et al.*[15] particular note was also taken of the associated "poststenotic dilatation," for which they advocated resection. Gudbjerg and Petersen,[18] after selectively visualizing the thoracic aorta and measuring the intra-arterial pressures proximal and distal to an apparent point of stenosis in 56 cases suspected of having coarctation of the thoracic aorta, found 4 patients who satisfied the criteria

of pseudocoarctation;[35] *i.e.*, there was dilatation of the ascending aorta with apparent aortic constriction at the arch, no luminal occlusion, and no collateral arterial circulation. Ross[29] and Šarić *et al.*[31] have also reported cases. Four new cases with congenital aortic stenosis (2 bicuspid aortic valves) and pseudocoarctation were recently reported from this Center.[39] Steinberg,[40] in 1962, last reviewed the subject and reported 8 new cases. Since then additional cases were reported by Stecken *et al.*,[34] Grismer and Weisburg,[17] Powell,[27] Beck,[6] Baert and Wellens,[2] Keller and Cheitlin,[21] Izukawa,[20] Nasser and Helmen,[24] Lochaya *et al.*,[22] and Griffin.[16] Turner and associates[44] reported aneurysm formation in the kinked aorta which was surgically resected.

EMBRYOLOGY

Pseudocoarctation seems to be closely related to true coarctation, the difference being that the aortic lumen is not compromised enough in a pseudocoarctation to cause a systolic pressure gradient across the narrowing. Pattinson and Grainger[25] have pointed out that Barry's[4] description of the complex changes that occur in the embryonic arch of the aorta during development may explain such aortic arch anomalies. In organogenesis some arterial segments elongate while others become greatly contracted; one of these changes occurs in the seventh dorsal intersegmental arteries when they undergo a cephalad shift and become the first portions of the subclavian arteries. When the heart descends into the thorax, the subclavian arteries remain relatively far cephalad; there is associated compression of the third to seventh segments of the dorsal aortic roots and of the left fourth aortic arch segments. Failure of compression of these segments during development results in an abnormally long arch of the aorta, which twists at the point of insertion of the ductus arteriosus or ligamentum arteriosum. Another explanation attributes the pseudocoarctation to a short, taut, ligamentum arteriosum[19,23,39] or patent ductus arteriosus. Both mechanisms may be involved. Elongated aortic arches and left subclavian arteries have been demonstrated in some of the cases in this series, as has relief of the pseudocoarctation by dividing the adjacent patent ductus arteriosus.

The dilatation of the descending aorta just distal to the pseudocoarctation is probably due to the same pressure-flow relationships that account for dilatation distal to a narrowing in any other situation; *e.g.*, poststenotic dilatation of the pulmonary artery with valvular pulmonic stenosis of varying degrees of severity. Since there is no stenosis in pseudocoarctation of the aorta, the term "postconstrictive" dilatation is preferable to "poststenotic" dilatation and indeed would apply to all degrees of localized narrowing of the aorta, with or without a pressure gradient.

Just as there may in the unusual patient be multiple sites of true coarctation of the aorta, so may there be multiple sites of pseudocoarctation, as illustrated by Cases VI and VIII. As the embryologic explanation for true coarctation of the aorta becomes clear, so will it be for pseudocoarctation.

PATHOLOGY OF PSEUDOCOARCTATION

Although a few patients with pseudocoarctation have come to postmortem examination, little is known about the pathology of or that associated with pseudocoarctation. One patient had bacterial endocarditis with intractable heart failure 7 years after the angiocardiographic diagnosis of pseudocoarctation, and, at postmortem examination the following year, a perforation was found in the cusps of the normally formed, tricuspid aortic valve.[40] Two patients had aneurysmal dilatation of the aortic sinuses.[18,35] Four patients had associated congenital aortic valvular stenosis, and in 2 of these the aortic valve was bicuspid. In Case V, a bicuspid, calcified, and stenotic valve was also found. Postmortem examination in one of the earlier reported cases revealed that parietal endocardial fibrosis and fibroelastosis had caused heart failure.[39] The 2 autopsied cases in the pres-

ent report had grossly visible kinking but no abnormality on microscopic study of the cells in the aortic wall.

ROENTGEN FEATURES OF PSEUDOCOARCTATION

Conventional roentgen studies, especially roentgenoscopy, contributed significantly to the diagnosis of pseudocoarctation but not to the differential diagnosis from true coarctation. In the frontal view, there may be an upper, rounded, pulsatile shadow, somewhat translucent owing to its position high in the left superior mediastinum (Fig. 10*A*). Immediately below, there is a more opaque rounded shadow which is usually upwardly convex and which begins just beyond or at the origin of the left subclavian artery. This vessel is dilated and tortuous and resembles the poststenotic dilatation of the descending aorta of a true coarctation. The left anterior oblique and lateral views are valuable in revealing the dense dilated lower shadow (which may be calcium-lined in adults) as the descending aorta. This dilated descending aorta also produces indentation of the esophagus in frontal and left anterior-oblique views, as with true coarctation. Even in the adult there is no rib notching from collateral circulation. This suggests that the aortic narrowing is not severe but does not distinguish a mild coarctation from pseudocoarctation.

ANGIOCARDIOGRAPHY

Angiocardiography provides the most reliable data regarding anomalies of the arch of the aorta. Opacification of the arch clearly identifies the structures that are included in the aortic deformity. Associated lesions such as those illustrated in this report can be readily demonstrated by contrast visualization combined with cardiac catheterization.

DIFFERENTIAL DIAGNOSIS

The differentiation of pseudocoarctation from true coarctation depends upon roentgen study together with measurement of pressure proximal and distal to the constriction. The absence of collateral arteries, especially on angiocardiograms, may be the only roentgenologic finding which favors the diagnosis of pseudocoarctation. Hemodynamic data showing absence of hypertension in the arms and no systolic pressure differential between the arms and legs are then necessary to ratify the diagnosis definitively.

Owing to the prominence of the malformed arch of the aorta, one may get the impression from the conventional roentgenogram of a tumor in the left superior mediastinum. The literature contains several references to cases in which exploratory thoracotomy and radiation therapy were carried out on the basis of such a mistaken diagnosis.[22,30]

Aneurysms of the arch of the aorta, especially those due to arteriosclerosis and trauma, also must be differentiated from pseudocoarctation. The arteriosclerotic aneurysms, usually saccular, are not difficult to diagnose because of their large size and the linear calcific material in their walls.[41] In the case of dissecting aneurysm, a double channel may be visualized. Patients with traumatic aneurysms at the top of the aorta usually have a history of severe chest trauma.[36,37]

Other anomalies of the arch of the aorta include those vascular rings which may cause dyspnea or dysphagia. A diverticulum in a right aortic arch can easily be identified on the esophagogram and by angiocardiographic studies.[26] Tumors in the superior mediastinum near the arch of the aorta may sometimes transmit pulsations, but in such instances, angiocardiography will readily establish the diagnosis.

SIGNIFICANCE OF DIAGNOSIS OF PSEUDOCOARCTATION

The diagnosis of pseudocoarctation is not merely of theoretic interest. Bacterial endocarditis may develop at the site of aortic narrowing or on the associated aortic valvular or other cardiac anomaly. It is important to protect such patients with antibiotics at times of predictable risk of endo-

carditis. Since aortic obstruction is absent in pseudocoarctation, surgical treatment of an uncomplicated pseudocoarctation is not indicated.

SUMMARY AND CONCLUSION

Pseudocoarctation of the arch of the aorta is an uncommon congenital anomaly which is anatomically similar to coarctation except that significant aortic obstruction is absent. Consequently, hemodynamic abnormalities do not occur; the blood pressures in the arms and legs are normal and collateral circulation does not develop. In the conventional roentgenogram, there may be signs similar to those of true coarctation. Angiocardiography delineates the unusually dilated and deformed arch of the aorta and demonstrates that the lower shadow is actually the dilated ("postconstrictive") descending aorta.

Terms proposed for this anomaly of the arch of the aorta, such as "kinking," "buckling," or subclinical coarctation, do not clearly differentiate this anomaly from true coarctation. Dilatation of the descending portion of the aorta, called poststenotic dilatation in the case of coarctation, also occurs in pseudocoarctation despite the absence of a stenosis. Accordingly, it would appear that dilatation of the descending aorta in pseudocoarctation is an integral feature of the malformation—another feature in which "pseudo" and "true" coarctation resemble each other. The term postconstrictive dilatation is suggested as being applicable to both situations. The malformation of the descending aorta without pressure gradient is at one pole of the spectrum of severity of coarctation of the aorta, the range being from this insignificant narrowing up to such an extreme degree as atresia or complete interruption of the isthmus of the aorta.

Except for 2 patients with aneurysmal dilatation of the aortic sinuses and 5 patients with aortic stenosis, associated congenital anomalies of the aorta have not been often reported in pseudocoarctation. In these 10 new cases, aortic and subaortic stenosis, patent ductus arteriosus, ventricular septal defect, single ventricle, atrial septal defect, and anomalies of the branches off the aortic arch were associated with pseudocoarctation. Pathologic and histologic studies of the first patient demonstrated that the pseudocoarctation was closely related to traction by the obliterated ductus arteriosus. The release of kinking by division of the patent ductus arteriosus in 2 patients also underscores this relationship and suggests the possible pathogenesis of the condition.

When murmurs at the base of the heart are heard in patients with pseudocoarctation, a bicuspid aortic valve, aortic stenosis, or turbulence owing to kinking of the aorta should be suspected. For these reasons, as well as the possibility of bacteria lodging in the deformed descending aortic arch or on a silent patent ductus arteriosus, prophylactic antibiotic therapy is recommended for oral or genitourinary surgical procedures.

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The selective angiocardiographic studies were made by Dr. Harry R. Stein and Dr. Richard Fleming.

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FATE OF RIB NOTCHING AFTER CORRECTION OF AORTIC COARCTATION*

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NOTCHING of the ribs secondary to augmented intercostal arterial collateral flow in coarctation of the aorta is a traditional roentgenologic sign. Few publications discuss the effect of correction of the coarctation on this notching. To our knowledge, only 1 case report, in 1954, by Jones and Steinbach,[6] has described regression of rib notching. In that instance, the notching regressed 1 year after surgical correction in a 14 year old boy (Fig. 1, *A* and *B*). In the major textbooks, discussions of coarctation do not mention this tangential aspect of the entity.

MATERIAL AND RESULTS

Serial roentgenograms of the chest were reviewed of 128 patients in whom a coarctated aorta had been corrected surgically. An end-to-end anastomosis of the thoracic aorta was accomplished in all patients after resection of the coarctated segment. Only 18 of these patients had unequivocal rib notching on preoperative roentgenograms and also had follow-up roentgenograms over an appreciable length of time. The ages of the 18 patients at the time of operation ranged from 8 months to 42 years (Table 1), including 2 younger than 2 years and 2 older than 20 years of age. In 7 of the 18 patients, notching regressed noticeably or disappeared completely within 6 months to a year after surgical correction. In 9 of the 18, moderate to slight regression was manifested, and in 2 of the 18 severity of the notching did not change. These 2 patients were 40 and 42 years old at the time of the operation.

DISCUSSION

Notching of the ribs is not pathognomonic of coarctation of the aorta, although

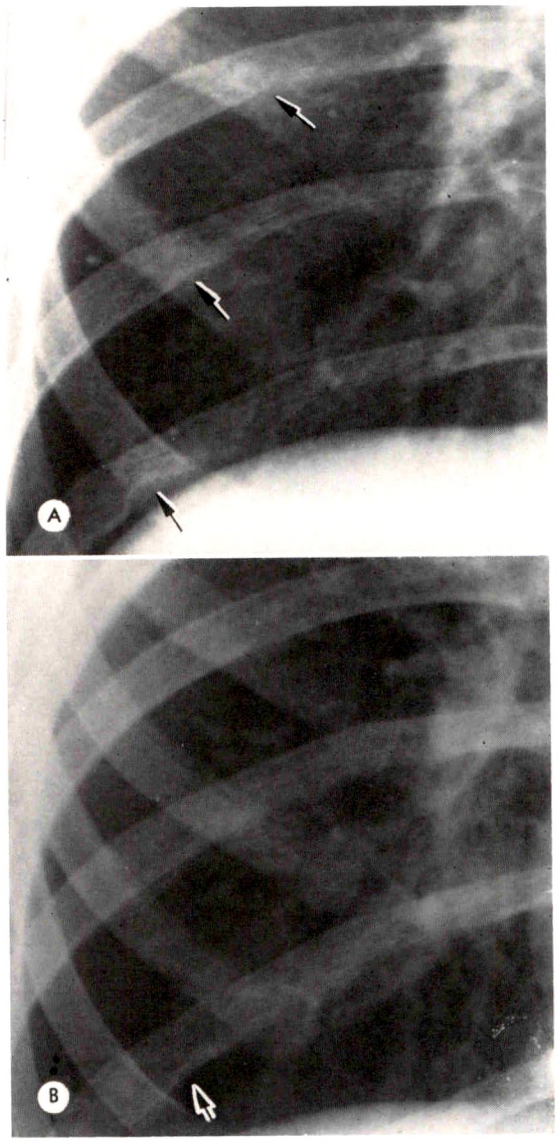


FIG. 1. (*A*) A 14 year old boy with coarctation of the aorta. Detailed view of the preoperative roentgenogram of the chest demonstrates notching of the right seventh, eighth, and ninth ribs. (*B*) Seven and one-half months after resection, the notches in the seventh and eighth ribs have disappeared. The notch in the ninth rib is still present but is considerably smaller.

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TABLE I

EFFECT OF REPAIR OF AORTIC COARCTATION ON RIB NOTCHING

Case No.	Age at Surgery/Sex	Number of Notched Ribs	Degree of Notching (+ ++ +++)*	Follow-up	
				Time Since Surgery	Appearance of Notch
I	8 mo./M	2	+	1 yr.	Disappeared
II	22 mo./M	1	++	4 yr.	Disappeared
III	3½ yr./M	1	++	1½ yr.	Disappeared
IV	9 yr./M	6	++ to +++	14 yr.	Disappeared
V	9½ yr./M	3	+	22 mo.	Disappeared
VI	4 yr./M	4	++	8 yr.	Marked regression
VII	14 yr./M	4	++ to +++	7½ mo.	Marked regression
VIII	2½ yr./M	2	+	11 mo.	Moderate regression
IX	7 yr./M	4	++	2½ yr.	Moderate regression
X	8 yr./M	2	++	7 mo.	Moderate regression
XI	10 yr./M	2	+	21 mo.	Moderate regression
XII	13 yr./F	5	++	4 yr.	Moderate regression
XIII	9 yr./F	3	++	4 mo.	Slight regression
XIV	12 yr./F	4	+	16 mo.	Slight regression
XV	12 yr./F	2	++	2 yr.	Slight regression
XVI	19 yr./F	3	++	19 mo.	Slight regression
XVII	40 yr./M	11	++	4 yr.	No change
XVIII	42 yr./F	8	+++	9 yr.	No change

* + = slight.
++ = moderate.
+++ = marked.

it is commonly associated with this entity.[1] Rib notching was first observed by Meckel in 1827[9,12] in a pathologic specimen, 36 years after the initial description of coarctation by Paris.[4,11] Roesler's report[13] in 1928, is still cited as containing the classic description of rib notching.[3]

Rib notching, when present, is usually bilateral, unless the coarctation is proximal to the origin of the left subclavian artery; in the latter instance only the right side manifests notching. Unilateral rib notching on the left may be seen when an aberrant right subclavian artery originates distal to the coarctation.[5] Notching is rare in the upper 2 ribs, since the first 2 intercostal arteries derive their blood supply from aortic branches proximal to the usual coarctation. The tenth and eleventh posterior intercostal arteries do not anastomose with the anterior branch of the internal mammary artery. Instead, they join the epigastric branches of the external iliac arteries and hence their associated ribs are not usually notched. Essentially, the twelfth intercostal is a lumbar artery.

With rib notching, the anterior rib segments are not affected. The anterior intercostal arteries are bifid and do not run in the subcostal groove as do the posterior intercostal arteries. The superior border of the ribs may become notched if tortuosity of the superadjacent posterior intercostal artery is so great that it makes contact with the rib below.[14]

Rib notching is rare in infancy. Caffey[2] stated that costal erosions are always absent in the first year of life. Levin and Rigler,[7] however, reported 1 patient seen at the age of 8 months and Neuhauser[10] reported another at 19 months. In 1 of our patients, notching of 2 ribs was seen at the age of 8 months. Surprisingly, Martelle and Moss[8] described notching in 13 per cent of infants younger than 1 year.

The regression and disappearance of rib

notching in our patients after repair of the coarctated aorta probably result from decrease in the size or the amplitude of pulsation of the intercostal arteries which functioned as collateral vessels. Remodeling of the rib, which occurs with growth, obliterates the impression on the ribs caused by the enlarged vessels. In younger patients, in whom bone growth is most rapid, the remodeling process is particularly efficient.

SUMMARY

The fate of rib notching after the correction of aortic coarctation has been investigated retrospectively in 18 patients. In 7 of the 18, notching regressed markedly or disappeared completely within 6 months to 1 year after surgical correction. In only 2, both in their forties at the time of operation, did the severity of the notching fail to improve. In younger patients with more rapidly growing bone, remodeling with obliteration of the notching is more rapid and more pronounced.

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THE THICKNESS OF THE LATERAL WALL OF THE LEFT VENTRICLE IN CONGENITAL HEART DISEASE

ANGIOCARDIOGRAPHIC DETERMINATION*

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ANATOMIC changes in the left ventricle may affect the width of the anterior, posterior, and lateral walls of this chamber, or of the muscle at the ventricular septum in cases of congenital heart disease. These changes may be related to obstruction of the blood flow or to right-to-left or left-to-right shunts at different levels and, consequently, to the increase or decrease in the cardiac output.

If we know the normal values (referred to a reliable variable), we may determine the thickness of the lateral wall of the left ventricle angiocardiographically. Quantitative angiocardiography has proven to be reliable for studying the effect of congenital or acquired cardiac diseases in the structure of the heart. The late phase of venous angiocardiogram or the left ventriculogram enables us to measure, in anteroposterior projection, the thickness of the lateral wall at the end of the ventricular diastole.

The purpose of this paper is to find the measurements of this wall in normals and in four of the most common types of congenital cardiac lesions. These results may be compared with studies made on postmortem specimens although at autopsy many factors are present and some differences may be anticipated between measurement made in the living and the cadaver.

MATERIAL AND METHODS

The hearts of 14 persons having no cardiac disease and 83 persons who had various types of congenital heart lesions were studied. In routine cardiac catheterization a No. 6 or 7 Cournand electrode catheter was used to obtain pressure levels and blood samples.

Immediately following the hemodynamics studies, the catheter was withdrawn, and a No. 6, 7, or 8 Lehman catheter with NIH tip was introduced. A Cordis angiographic injector was utilized to inject the contrast medium intracardially into the lower part of the cavity of the right atrium, inflow tract of the right ventricle, or the main pulmonary artery. The pressure ranged from 300 to 700 lb./inch^2. From 1.0 to 1.5 ml. of 75 per cent hypaque was injected in each instance, during approximately 1 or $1\frac{1}{4}$ seconds. In all cases, simultaneous recording of the electrocardiogram and roentgen-ray exposure was made (Sanborn Poly-Viso).

Angiocardiograms were made with a maximum of 25 or 30 exposures, at a speed ranging from 3 to 5 per second, employing a 14 by 14 inch Schönander film-changer with a fixed tube-to-target distance of 36 inches. A proper field corresponding to the thorax was circumscribed with a Siemens collimator. In all cases, the opaque medium was injected while the patient was lying supine on a thick, spongy pad on the roentgenographic table.

Correction for distortion was determined individually in every case. The measurement of the width of the lateral wall of the left ventricle was made 1 cm. above the

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apex and at its mid-portion, and only in the anteroposterior projection at the end of diastole. Systemic and pulmonary blood flows were determined by the Fick principle.

NORMAL CASES

In the hearts of 14 persons who had no cardiac lesions, a direct relationship was found between the thickness of the free wall of the left ventricle, measured at the apex, and at the mid-portion, and the B.S.A. ($m.^2$) (Fig. 1).

Apex:

$$Y = a + bX = 2.186 + (3.635)X \quad r = 0.98$$

Mid-portion:

$$Y = a + bX = 2.6209 + (4.3566)X \quad r = 0.93$$

CONGENITAL CARDIAC DISEASE

A. MEASUREMENT OF THE FREE WALL AT THE APEX

The respective linear regression equations are:

V.S.D.:

$$Y = a + bX = 4.8759 + (1.1776)X \quad r = 0.38$$

A.S.D.:

$$Y = a + bX = 3.3861 + (2.0562)X \quad r = 0.81$$

P.S.:

$$Y = a + bX = 2.904 + (2.5405)X \quad r = 0.73$$

T. of F.:

$$Y = a + bX = 2.586 + (1.6132)X \quad r = 0.57$$

Ventricular septal defect. In 3 instances, there was evidence of high pulmonary vascular resistance; 2 presented significant degree of mitral insufficiency; and 7 pulmonary stenosis of slight degree.

The scattergram illustrated in Figure 2 is a plotting of the thickness of the free wall against the B.S.A. ($m.^2$), which indicated that 12 of the 33 observations (36 per cent) presented values above normal. Figure 3 shows a heart with a huge left ventricular cavity and a large pulmonary flow index ($L/min./m.^2$).

Atrial septal defect. In 2 hearts, the findings were consistent with high pulmonary resistance; 9 had various types of partial anomalous drainage of the pulmonary veins.

SURVEY OF MATERIAL AND SUMMARY OF RESULTS

Lesion	No. of Cases	B.S.A. ($m.^2$)		Thickness (mm.)		S.B.F. (L/min.)		P.B.F. (L/min.)	
		Range	Ave.*	Range	Ave.*	Range	Ave.*	Range	Ave.*
MEASUREMENTS MADE AT THE APEX									
Normal	14	0.62–2.00	1.09	4.6–7.0	5.9	—	—	—	—
V.S.D.	33	0.64–1.80	0.96	4.6–7.5	6.0	1.9–7.3	3.7	3.6–23.9	7.9
A.S.D.	23	0.63–1.44	1.00	4.1–6.6	5.4	2.0–6.1	3.7	2.9–22.0	9.1
P.S.	21	0.62–1.80	1.15	4.1–8.4	5.8	2.4–5.3	3.7	2.1– 6.5	3.8
T. of F.	6	0.74–1.55	0.93	3.3–5.3	4.0	2.2–6.4	4.4	1.7–3.7	2.8
MEASUREMENTS MADE AT THE MID-PORTION									
Normal	14	0.62–2.00	1.09	5.4–12.0	7.4	—	—	—	—
V.S.D.	33	0.64–1.80	0.96	6.0–14.0	9.4	1.9–7.3	3.7	3.6–23.9	7.9
P.S.	21	0.62–1.80	1.15	5.5–10.4	7.9	2.4–5.3	3.7	2.1–6.5	3.8

List of abbreviations: V.S.D. = ventricular septal defect; A.S.D. = atrial septal defect; P.S. = pulmonary stenosis; T. of F. = tetralogy of Fallot; B.S.A. = body surface area ($m.^2$, square meter); S.B.F. = systemic blood flow (L/min., liters per minute); P.B.F. = pulmonary blood flow (L/min.) and * = average.

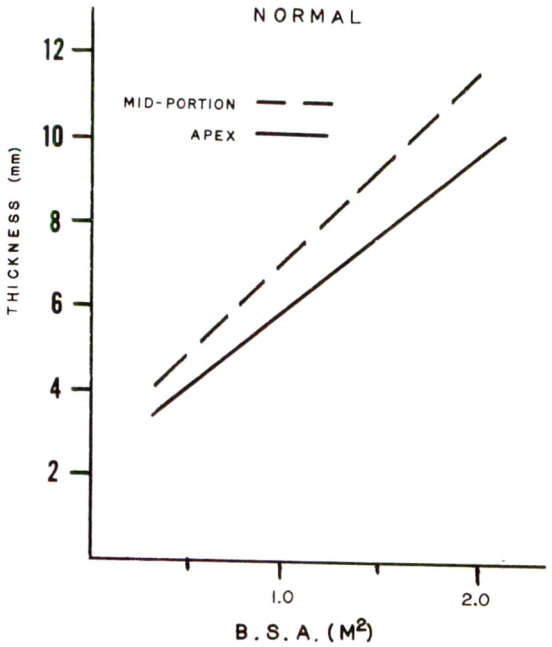


FIG. 1. Normal regression line obtained when the measurements of the thickness of the lateral wall of the left ventricle at the apex and at the mid-portion were correlated to the B.S.A. (m.²).[2] B.S.A. = body surface area.

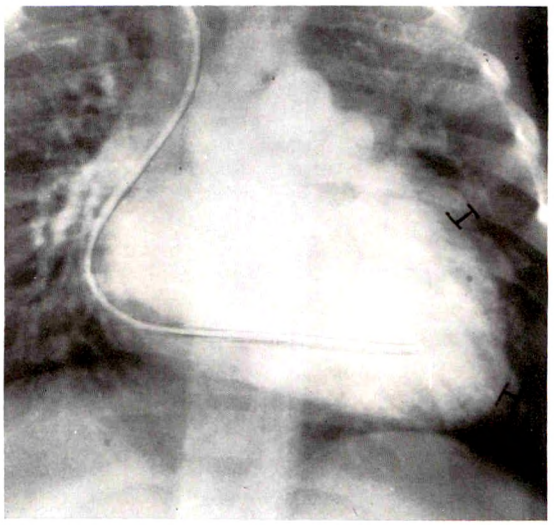


FIG. 3. Selective venous angiocardiogram, in levo phase, at end-diastole, in a heart having a ventricular septal defect, exhibiting a greatly enlarged left ventricular cavity. The ascending aorta is small, and the pulmonary trunk displays re-opacification. The B.S.A. was 1.41 m.². Thickness of lateral wall at the apex was 5.2 mm.; and at the mid-portion 9.5 mm. (Normal values are 7.5 mm. and 8.9 mm., respectively.) P.F.I. 17 L/min./m.². P.F.I. = pulmonary flow index.

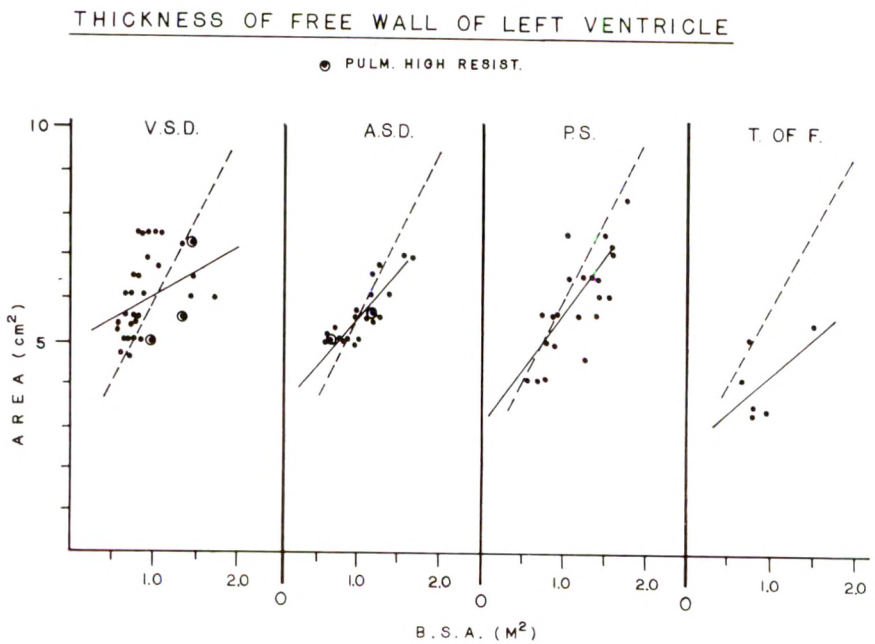


FIG. 2. Correlation between the measurements of the thickness of the lateral wall of the left ventricle at the apex and the B.S.A. (m.²). Broken line indicates normal regression line; solid lines indicate regression line for each group of cases of congenital heart disease. There is direct relationship between the two parameters. V.S.D. = ventricular septal defect; A.S.D. = atrial septal defect; P.S. = pulmonary stenosis; T. of F. = tetralogy of Fallot.

The scattergram of Figure 2 indicates that the values were above normal in 10 of 23 cases (43 per cent). Figure 4 demonstrates a case of ostium secundum type of defect in which the typical pattern of the levo-angiocardiogram is present.

Pulmonary stenosis. Five instances manifested the infundibular type of defect and 1 was associated with an atrial septal defect; 4 cases presented patent foramen ovale and one of them, in addition, valvular aortic stenosis.

The scattergram of Figure 2 indicates that 4 of 21 cases (19 per cent) had values above normal.

Tetralogy of Fallot. This group comprises patients with different degree of severity.

The scattergram of Figure 2 reveals that all cases except one (83 per cent) had values below normal.

The normal regression line was compared with the regression line of each group of congenital heart diseases studied (Fig. 5). In all these groups a direct relationship was found, but the regression line of the normal cases was steeper and more elevated. The regression lines in the others were in order of decreasing frequency: P.S., A.S.D., V.S.D., and T. of F.

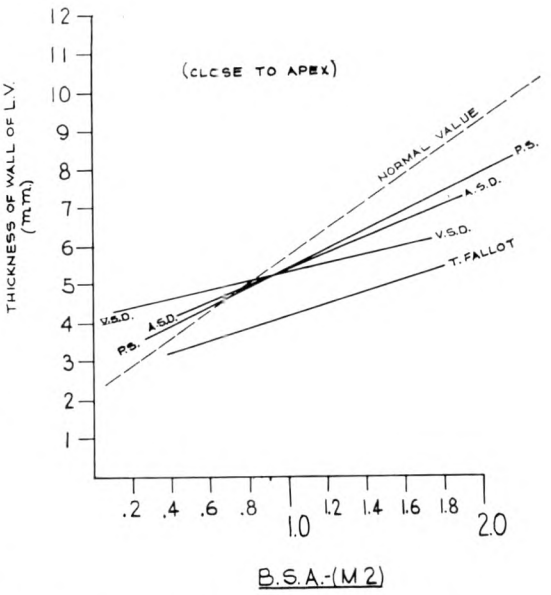


Fig. 5. Regression line of thickness of the left ventricle at the apex correlated with the B.S.A. ($m.^2$), indicates a direct relationship among the four groups of congenital heart disease considered.

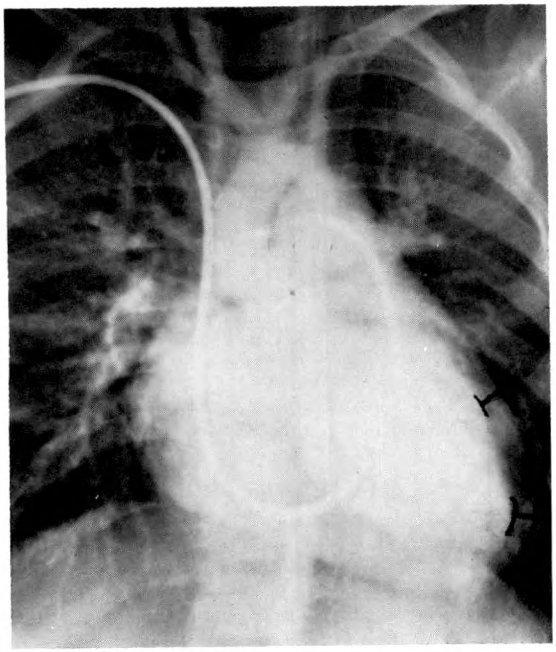


Fig. 4. Selective venous angiocardiogram in the levo phase of a heart with an atrial septal defect of the ostium secundum type. Re-opacification of the right atrium, right ventricle, and pulmonary artery. B.S.A. was 0.68 $m.^2$. Thickness of the lateral wall at the apex was 6.1 mm.; and at the midportion 6.1 mm. (Normal values are 4.8 mm. and 5.7 mm., respectively.) P.F.I. 10 L/min./$m.^2$.

As may be noted, the higher the calculated value of the B.S.A. ($m.^2$) in the observations that were made, the greater the distance between the normal regression line and that for each group considered.

Correlation of measurements made at the apex with the systemic blood flow (L/min.). From these data, the thickness of the free wall was plotted (Fig. 6). No relationship whatever was found between the two values in V.S.D.; in A.S.D., there appears to be a tendency toward an inverse relationship; in P.S., a direct relationship was found; and in T. of F. also, a tendency to a direct relationship can be seen. The greater values of systemic blood flow found in P.S. can be explained on the basis of a higher average of the B.S.A. ($m.^2$). Lower values are present in T. of F. and, in fact, the lowest val-

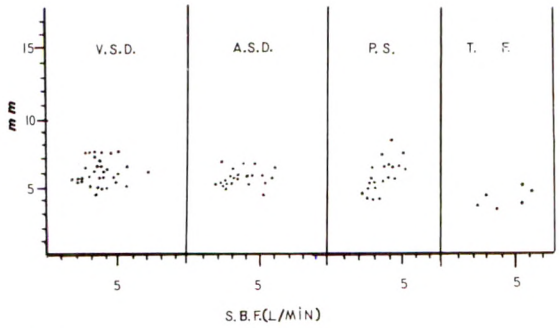


FIG. 6. Thickness of the lateral wall of the left ventricle at the apex is correlated with the S.B.F. (L/min.) of the four groups of congenital heart disease considered. Note that the values are higher in the group with pulmonary stenosis and lower in the group with tetralogy of Fallot. S.B.F. = systemic blood flow.

ues of B.S.A. ($m.^2$) were found in this anomaly.

B. MEASUREMENT MADE AT THE MID-PORTION

Measurement was made at the mid-portion in V.S.D. as an example of left-to-right shunt, utilizing pulmonary stenosis as a representative lesion in which pulmonary circulation is restricted (Fig. 7). When values were plotted against the B.S.A. ($m.^2$), a striking difference was noted in these cardiac lesions. In cases of V.S.D., the linear regression line made may be expressed as follows:

$$Y = a + bX = 5.5382 + (4.0938)X \quad r = 0.47.$$

In V.S.D. marked scattering of values was present. The results were more uniform in P.S., but the values were by far below the ones found in V.S.D.

Correlation of measurements made at the mid-portion with the systemic blood flow (L/min.). Only V.S.D. and P.S. were considered in this study; the former as representative of lesions having a restricted pulmonary circulation. No significant relationship was found to be present in this study, but higher values were found in V.S.D. It should also be noted that cases of V.S.D. with high pulmonary resistance tend to have lower values (Fig. 8).

Correlation of the measurements made at the apex with the pulmonary blood flow (L/min.). Figure 9 demonstrates that no significant relationship appears to be present in cases of ventricular septal defect and atrial septal defect. In pulmonary stenosis and tetralogy of Fallot, a direct relationship was found.

Correlation of the measurement made at the mid-portion with the pulmonary blood flow (L/min.). Figure 10 shows no correlation in cases of ventricular septal defect, but in pulmonary stenosis, excluding the case associated with the atrial septal defect, a direct relationship was revealed between both parameters. A finding that deserves to be emphasized is that numerous values in pulmonary stenosis were lower than in ventricular septal defect. In the latter, a thicker lateral wall of the left ventricle was found either in small or large pulmonary blood flow.

DISCUSSION

Upon reviewing the scant medical literature pertaining to this subject, it is evident that there are great differences owing to the diversity of criteria that have been adopted. The thickness of the free wall of this chamber has been determined at various sites: apex, mid-portion, or at the

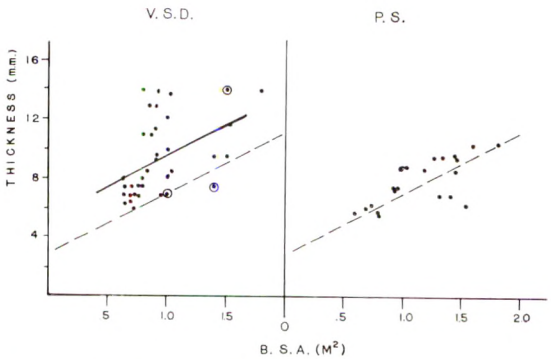


FIG. 7. Thickness of the free wall of the left ventricle at the mid-portion is correlated with the B.S.A. ($m.^2$) in the group of cases of ventricular septal defect and pulmonary stenosis. Broken line is the normal regression line; solid line is the regression line for ventricular septal defect. Note that in the latter disease the majority of the observations appear to be above the normal regression line.

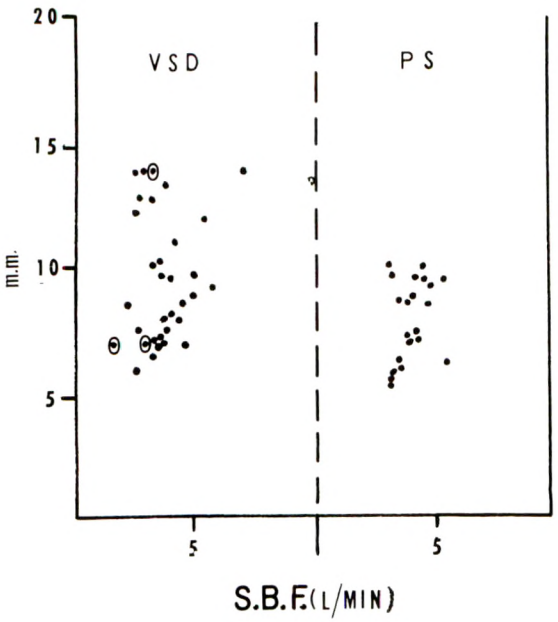


Fig. 8. This scattergram is a plotting of the width of the mid-portion of the parietal wall of the left ventricle and the S.B.F. (L/min.). The circles indicate the value for cases of ventricular septal defect with pulmonary high resistance.

thickest part of any region. Measurements have also been made in living persons and in preserved specimens or fresh hearts of cadavers; the cause of death is generally not stated in those cases with hearts designated as "normal."

The following factors, which may affect the cardiac measurement made in the cadaver, should be kept in mind: the direction of the anatomic section; the degree of contraction or relaxation of the cardiac muscle, even when it is fresh; and, moreover, some authors[7–12] have correlated the width of the wall to other variables such as age and weight.

de la Cruz *et al.*[3] determined the largest dimensions of the anterior, lateral, and posterior border of the left ventricle in normal fresh cadavers.

Rowlatt *et al.*,[11] who studied the hearts of 783 children from birth to 15 years of age, made measurements of different parts of the left ventricle and established correlations of the thickness of the lateral wall

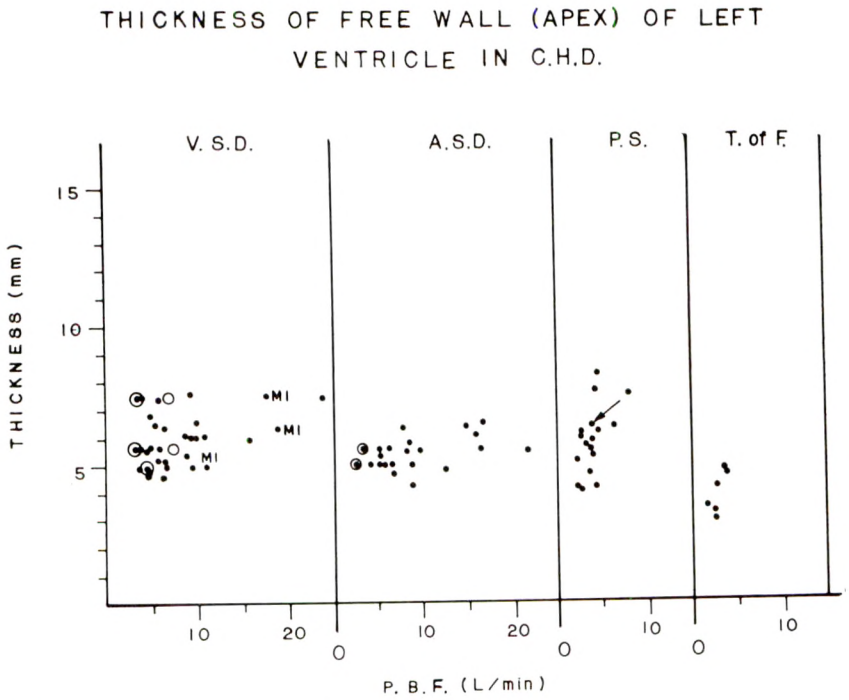


Fig. 9. Correlation between the thickness of the lateral wall of the left ventricle and the P.B.F. (L/min.). Note that only in pulmonary stenosis and tetralogy of Fallot appears to be a direct relationship. C.H.D. = congenital heart disease.

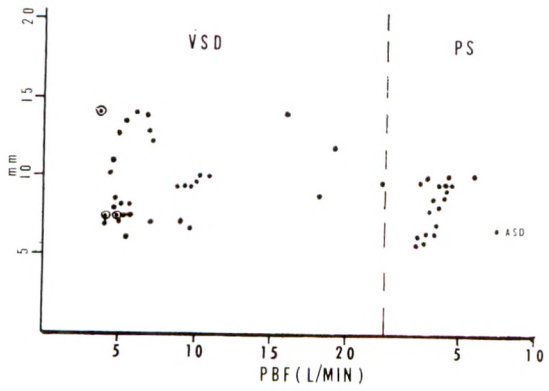


FIG. 10. Correlation between the thickness of the lateral wall of the left ventricle and the P.B.F. (L/min.) at the mid-portion. The circles indicate cases with high pulmonary resistance. In ventricular septal defect no relationship is present between the two parameters but in pulmonary stenosis there is a direct relationship.

with age, weight, height, and surface area of the child.

In the living person, it is possible to determine the thickness of the left ventricular wall at any moment of the cardiac cycle; it is evident that in the frontal projection at the end of the diastole, it may be measured very accurately. Unfortunately, this method has not been proved to be useful for determining the anterior and posterior walls.

Levine *et al.*,[9] Castellanos and Hernandez,[2] and Hatam *et al.*[6] angiocardiographically measured the width of the lateral wall of this cavity in aortic diseases and among normal children.

It is very important to emphasize the fact that we do not estimate the width of the left ventricular wall in relation to the size of the heart, but to the B.S.A. (m.^{2}); in some cases of gross cardiomegaly, for example, the thickness of this wall appears to be smaller when compared to the size of the heart or to the diameter of the thorax; however, when correlated to the B.S.A. (m.^{2}) it may be slightly above the normal.

The direct relationship found in normal hearts and those with congenital heart disease of the apex and at the mid-portion is related to its proportional increase in size with the body growth.

In V.S.D. the width of this wall usually is overlooked in the medical literature.[4,10] Only Keith *et al.*[8] alleged that in this disease the wall of the left ventricular cavity is thicker than normal.

The comparison of the normal regression line with those of the four groups of congenital cardiac malformations indicated in Figure 6 reveals that the lowest values are found in tetralogy of Fallot. In V.S.D., the regression line appears to be above the normal when the B.S.A. is above 0.80 m.^{2}, which corresponds approximately to 7 years of age. However, in the mid-portion, we found that with the exception of 4 instances, all of them were above the normal regression line. When the measurements were made at the mid-portion, 94 per cent of the cases of V.S.D. and only 67 per cent of those with P.S. presented values above the normal when correlations were made with the B.S.A. (m.^{2}). When correlations were made with the P.B.F. (L/min.) at the same site we found that 30 per cent of the cases of V.S.D. presented higher thickness values than those of P.S. However, no significant relationship was found between the thickness of the lateral wall and the amount of blood flowing through the aorta.

Because the higher the P.B.F. (L/min.), the larger the left-to-right shunt, we may draw the conclusion that a large left-to-right shunt may be found with moderate thickening of the lateral wall of the left ventricle, and that a small shunt may be found with the normal or thick left ventricular wall. This means that the width of this wall in V.S.D. does not depend only on the importance of the left-to-right shunt. Other factors may influence the width of it in this disease; for instance, in some patients, the shunt sometimes decreases as the patient grows older. Obviously, association to other cardiac lesions should be considered.

At any rate, we may conclude that measurement of the thickness of the mid-portion of the lateral wall of the left ventricle much better expresses the abnormalities of the architecture of the cardiac musculature

than does measurement at the apex of this chamber in the types of congenital heart disease we have studied in this article.

CONCLUSIONS

(1) The thickness of the free wall of the left ventricle in the hearts of 14 normal persons and of 83 patients with various types of congenital heart disease was determined angiocardiographically at the end of diastole in the anteroposterior projection. The congenital cardiac malformations included: V.S.D. (33); A.S.D. (23); P.S. (21); and T. of F. (6). Measurements of the left ventricle were made at the apex and at the mid-portion of the lateral wall, and the results were correlated with the B.S.A. ($m.^2$): 36 per cent of the cases of V.S.D., 43 per cent of A.S.D., 19 per cent of P.S., and 17 per cent of T. of F. had values above the normal when the width of the lateral wall was measured at the apex; 94 per cent of the cases of V.S.D. and 67 per cent of P.S. had values above the normal when measurements were made at the mid-portion.

(2) The pulmonary blood flow (L/min.) and the systemic blood flow (L/min.) were correlated with the width of the lateral wall of the left ventricle at its apex and its mid-portion: 30 per cent of the cases of V.S.D. presented greater thickness values than those of P.S. when correlations were made with pulmonary blood flow (L/min.) at the mid-portion. No significant correlation was found between the two parameters in cases of V.S.D., when the measurements were made at the apex. This finding has been discussed briefly.

(3) In the four groups of congenital cardiac lesions studied, the values obtained from measurements made in the mid-portion seem to express much better the effect of the hemodynamic changes on the cardiac musculature than do the values derived from the thickness of the heart at the apex.

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VENTRICULAR SEPTAL DEFECT ASSOCIATED WITH AORTIC INSUFFICIENCY*

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VENTRICULAR septal defect is a common congenital malformation. It is, however, rarely associated with aortic insufficiency. According to the literature the combination of these two lesions is present in approximately 3–5 per cent of all ventricular septal defects.[3,9,15] The aortic insufficiency arises as a complication of a ventricular septal defect which results in deficient support for the aortic cusps so that the latter prolapse into the left ventricular outflow tract. Pulmonary insufficiency due to the same mechanism has been described in two instances.[6,9]

In addition, obstruction to the right ventricular outflow is not uncommon in these patients and is due to infundibular or valvular pulmonic stenosis or prolapse of the aortic valve through the ventricular septal defect.[2,9,10]

Little attention has been given to this syndrome in the radiologic literature and only a few reports deal specifically with these cases.[1,11]

In this paper we report 10 patients with ventricular septal defect associated with aortic insufficiency with emphasis on the roentgenologic and angiocardiologic features.

ANATOMY

For the convenience of the reader the normal anatomic features will be briefly reviewed and some important landmarks defined (Fig. 1). The crista supraventricularis is a muscular prominence lying along the upper septal wall of the right ventricle and arching between the tricuspid and pulmonary rings. Two muscular bands of variable thickness, the septal band and the parietal band, arise from the crista supraventricularis. The septal band passes along the wall of the septum in an almost vertical direction to the apex. The parietal band is more oblique and passes along the anterior wall of the right ventricle. There are no corresponding structures on the left side of the septum.

The ventricular septum consists of 3 parts:

(a) The main, bulky part is the muscular septum.

(b) The bulboventricular portion forms the division between the outflow tracts of both

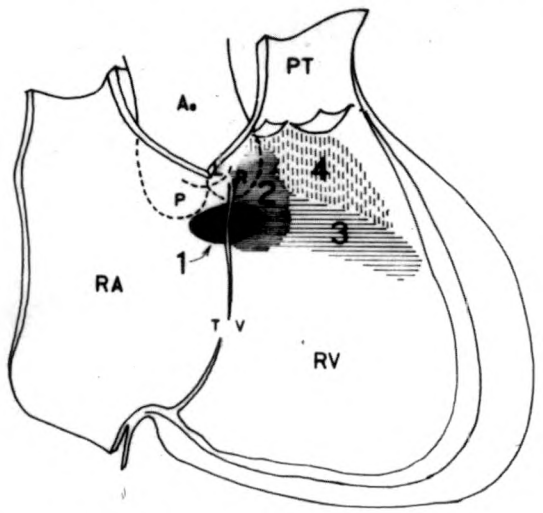


FIG. 1. Normal relationships of the membranous portion of the ventricular septum (1), crista supraventricularis (2), septal band (3), and the bulboventricular portion of the ventricular septum (4). Note how the membranous septum approximates the posterior aortic sinus (P) in its posterior part and the right aortic sinus (R) in its anterior part. Ao = ascending aorta; PT = pulmonary trunk; RA = right atrium; TV = tricuspid valve; RV = right ventricle.

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ventricles. It is continuous below and anteriorly with the muscular septum and reaches the pulmonary valve superiorly. On the left ventricular aspect, it forms the part of the ventricular septum below the commissures between the right and left aortic cusps.

(c) The membranous portion is variable in size but rarely larger than 1 cm. in diameter. Its anterior part is continuous with the posterior part of the bulbar septum. On the left ventricular aspect the membranous septum lies inferior to the commissures between the right and posterior aortic cusps. On the right ventricular aspect the membranous septum is posterior and inferior to the crista supraventricularis and hidden behind the septal and anterior leaflets of the tricuspid valve. Its lower border can be determined by the septal band of the crista supraventricularis. The septal leaflet of the tricuspid valve crosses the membranous septum obliquely. It is attached to this septum and divides it into an atrioventricular part localized superiorly and posteriorly and an intraventricular part localized anteriorly and caudally.

If the ventricular septal defect involves mainly the middle part of the membranous septum, there will be deficient support for the posterior and right aortic cusps and thus aortic insufficiency will involve these structures. If the ventricular septal defect is in the anterior portion of the membranous septum and part of the bulbar septum, the deficient support will involve mainly the right cusp.

In the 2 cases described in the literature in which the ventricular septal defect caused prolapse of the pulmonary valve,[6,9] the deficiency was more anteriorly located in the bulbar septum.

MATERIAL

Of a group of 387 patients with ventricular septal defect studied at the Heart Institute, 10 cases were found to be accompanied by aortic insufficiency of the type under discussion.

All of the patients underwent repeated roentgenologic examination. Right heart catheterization was performed in 9, selective thoracic aortography in 8, and left ventriculography in 3 patients. In 1 patient selective right ventriculography was performed.

CLINICAL DATA

Seven of the patients were males and 3 females; their ages ranged from 6 to 27 years. Congenital heart disease was diagnosed early in life in all patients. The initial clinical features were due to the ventricular septal defect; the characteristic systolic murmur was noted on routine examination at birth in 4 cases and within the first year of life in the remainder.

With the appearance of the aortic insufficiency, the diastolic murmur was a characteristic and outstanding feature on clinical examination. This murmur was not present in any of the cases before the age of 2 years. Other features of aortic run-off, such as the collapsing pulse, widening pulse pressure and signs of left ventricular hypertrophy, also became apparent. The initial electrocardiogram showed biventricular hypertrophy but, subsequently, all cases showed a predominant left ventricular hypertrophy pattern and in 6 of them a left ventricular strain pattern with negative T waves in left precordial leads was present.

FINDINGS ON RIGHT HEART CATHETERIZATION

Right heart catheterization was performed in 9 cases. In 6 of them the pressures in the right ventricle and pulmonary artery were in the region of the upper limits of normal, but in 1 case a gradient of 25 mm. Hg was found across the pulmonary valve. The remaining 2 cases showed elevated pressures in the right ventricle. In 1 case the pressure was 95 mm. Hg in the right ventricle and 25 mm. Hg in the pulmonary artery, and in the other case the pressure was 95 mm. Hg in the right ventricle but the pressure in the pulmonary artery could not be recorded for technical

reasons. In 1 case the oxygen saturation was normal in the lesser circulation. In the other cases a step-up of at least 5 per cent in oxygen saturation was present between the right atrium and right ventricle. The maximal step-up present was 16 per cent.

ROENTGENOGRAPHIC FINDINGS

The roentgenographic findings reflected the natural history of the disease and were dependent on the relative severity of the two components of the lesion. The over-all size of the heart, on initial examination, was considered to be markedly increased in 2 cases, moderately increased in 5 cases and only slightly increased in 3 cases (Fig. 2). Initially the cardiomegaly was due to biventricular enlargement. With the appearance of aortic insufficiency, the cardiomegaly was seen to be dominated by left ventricular enlargement in all cases. Left atrial enlargement was not a prominent feature in any of the cases, but slight enlargement was seen in 2 patients. Prominence of the ascending aorta on conventional roentgenograms was noted in 6 cases. The prominence of the pulmonary vasculature was related to the magnitude of the left-to-right shunt and was marked in 2 cases and moderate in the remainder.

One patient deserves special mention. At the age of 3 years a systolic-diastolic murmur was heard and biventricular enlargement was present clinically. The plain roentgenogram revealed moderate cardiomegaly. On the left heart border, the pulmonary segment was prominent and the aortic knob normal. The pulmonary vasculature was markedly increased (Fig. 3*A*). A diagnosis of patent ductus arteriosus was made and the ductus was ligated. Following the operation a systolic-diastolic murmur could still be heard. Follow-up roentgenograms during the subsequent years showed that the aorta became progressively dilated while the pulmonary vasculature decreased (Fig. 3, *B–E*). Ten years following the operation right heart catheterization was performed and a systolic pressure gradient of 60 mm. Hg was measured between the right ventricle and the pulmonary artery. Selective right heart cardioangiography, performed at the same stage, showed that the right ventricle was enlarged and that a polypoid mass was present at the infundibular region during systole (Fig. 4, *A* and *C*), whereas the outflow tract of the right ventricle had a normal appearance during diastole (Fig. 4, *B* and *D*). The mass was subsequently shown by selective thoracic aortography to have been produced by a prolapsed right aortic cusp (Fig. 4, *E* and *F*). The latter investigation also revealed aortic insufficiency of moderate degree and no definite left-to-right shunt could be seen. This was, therefore, a case of patent ductus arteriosus and ventricular septal defect in which the patent ductus arteriosus was ligated and the ventricular septal defect complicated by aortic insufficiency. The prolapse of the right aortic cusp eventually blocked off the ventricular septal defect and gave rise to obstruction of the right ventricular outflow tract.

SELECTIVE THORACIC AORTOGRAPHY

Selective thoracic aortography was performed in 8 cases and demonstrated aortic insufficiency of mild to moderate degree. This investigation also clearly showed which of the sinuses was involved in the production of aortic insufficiency. The dilatation involved the right sinus only in 1 case, both the right and the posterior sinuses in 4 cases, the posterior sinus only in no case and all the sinuses equally in 1 case.

When the right sinus was involved a characteristic step-like bulging was noted between the dilated upper part of the sinus and the ascending aorta. This bulging was best noted in the lateral aortograms (Fig. 5). In systole the dilated sinus descended and bulged anteriorly in the direction of the ventricular septal defect; the bulging, however, was most marked during diastole. This bulging of the right sinus was noted in more than half of the cases. In 3 of the cases in which dilatation of the posterior sinus was present, an additional pocket of

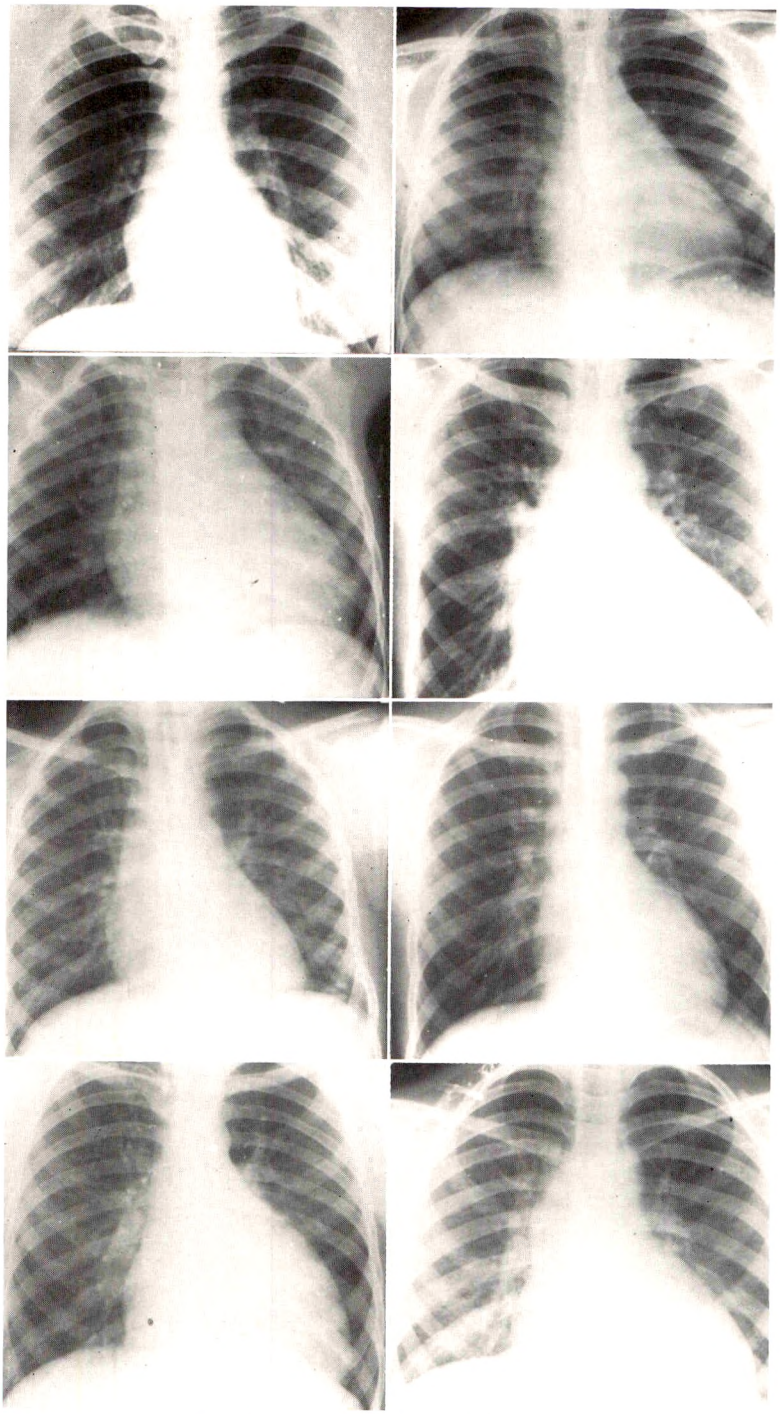


FIG. 2. Frontal roentgenograms of the thorax of various patients with ventricular septal defect and aortic insufficiency demonstrating cardiomegaly, prominent aortic arch and increased pulmonary vasculature.

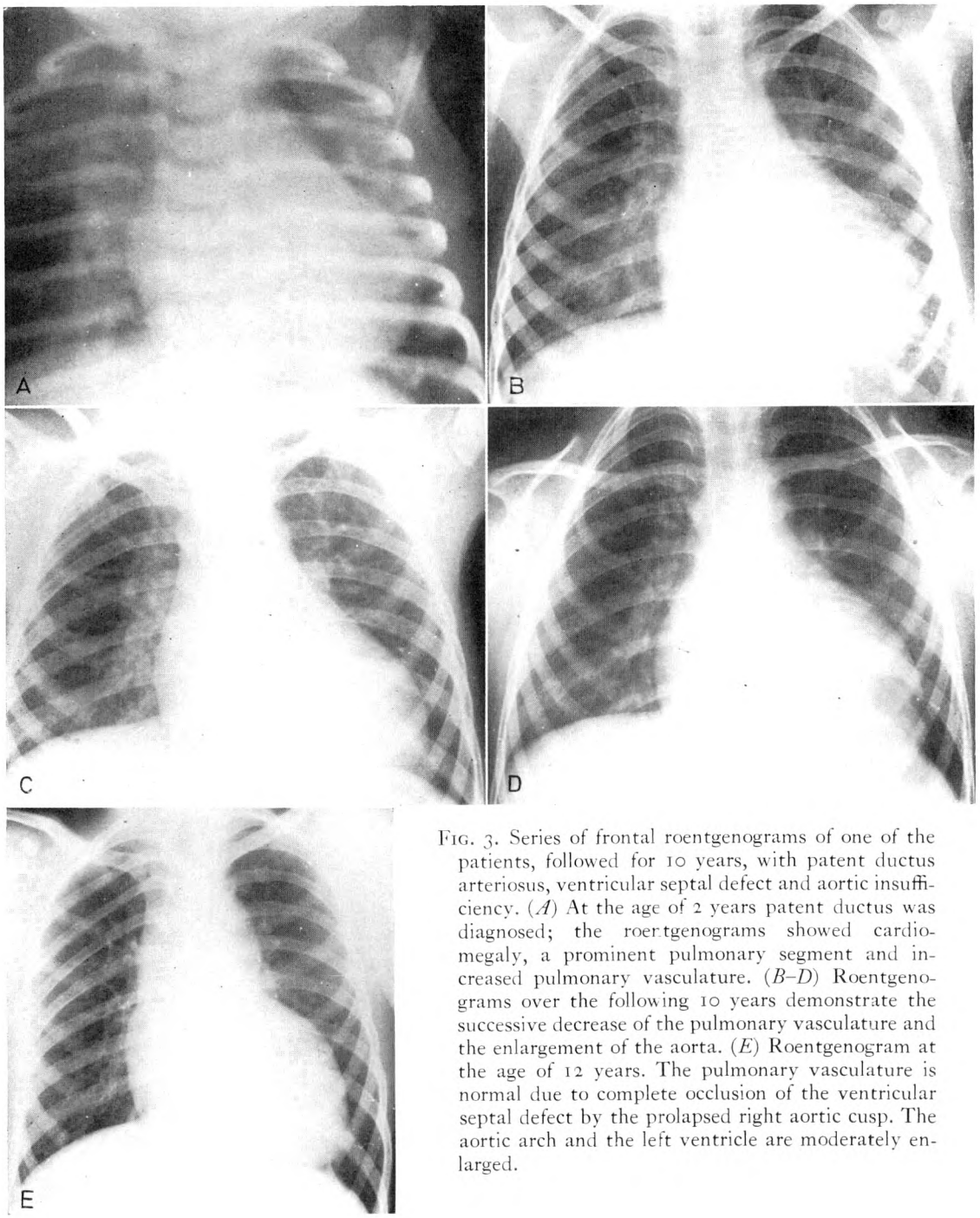


FIG. 3. Series of frontal roentgenograms of one of the patients, followed for 10 years, with patent ductus arteriosus, ventricular septal defect and aortic insufficiency. (*A*) At the age of 2 years patent ductus was diagnosed; the roentgenograms showed cardiomegaly, a prominent pulmonary segment and increased pulmonary vasculature. (*B–D*) Roentgenograms over the following 10 years demonstrate the successive decrease of the pulmonary vasculature and the enlargement of the aorta. (*E*) Roentgenogram at the age of 12 years. The pulmonary vasculature is normal due to complete occlusion of the ventricular septal defect by the prolapsed right aortic cusp. The aortic arch and the left ventricle are moderately enlarged.

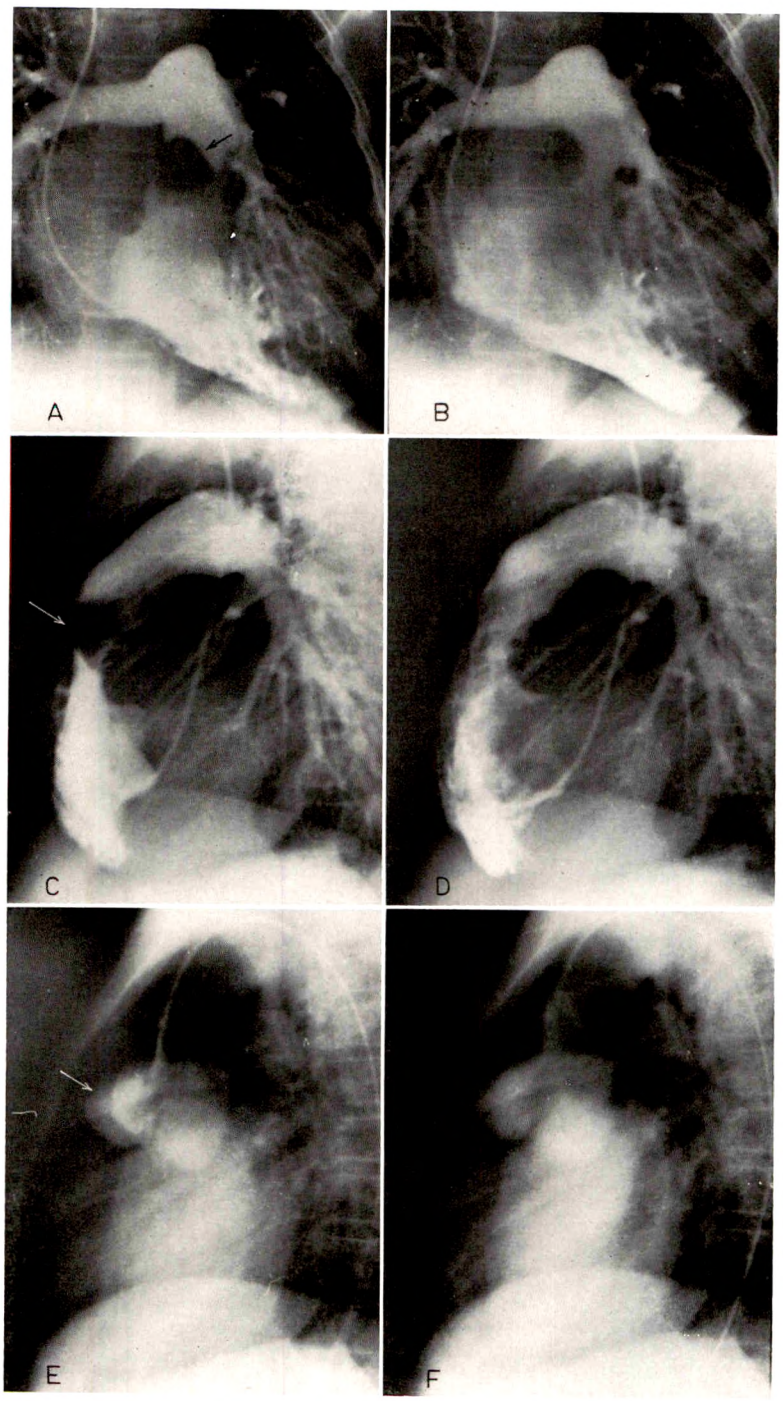


Fig. 4. Selective right ventriculography and thoracic aortography demonstrating right outflow tract obstruction caused by prolapse of the right aortic cusp into the right ventricular outflow tract (same patient as in Figure 3). (*A* and *C*) Selective right ventriculograms in systole, anteroposterior and lateral projections. A round filling defect is visualized in the outflow tract of the right ventricle (arrow). (*B* and *D*) Selective right ventriculograms in diastole, anteroposterior and lateral projections. The right ventricular outflow tract has a normal appearance. (*E*) Selective thoracic aortogram. In systole the prolapsed right aortic cusp bulges anteriorly (arrow) corresponding to the filling defect seen in *C*. (*F*) Selective thoracic aortogram. In diastole the prolapsed cusp is less prominent.

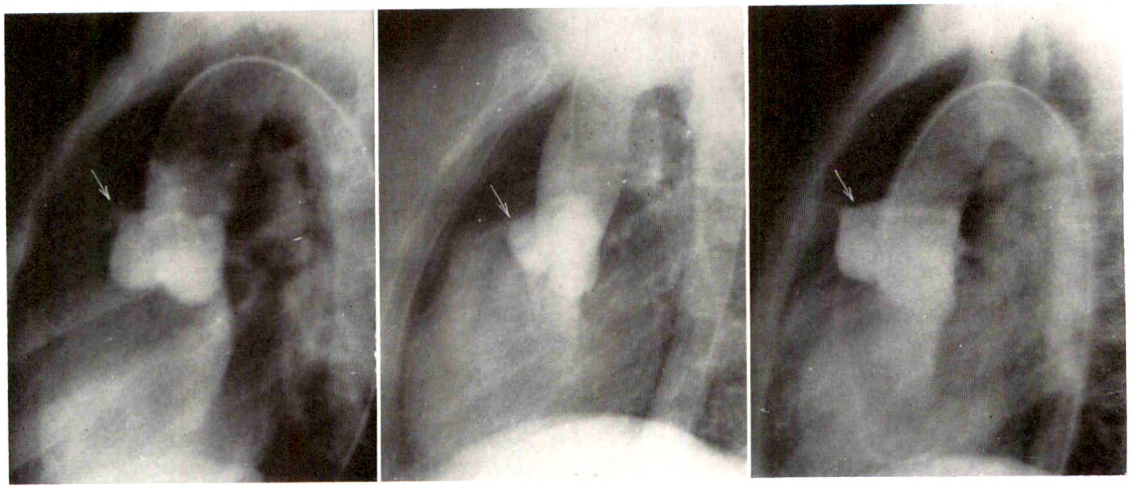


FIG. 5. Selective thoracic aortograms of various patients with involvement of the right aortic cusp. The characteristic step-like bulging of the right aortic sinus (arrow) and the anteriorly tilted aortic valve are demonstrated.

contrast material continuous with the sinus could be seen (Fig. 6); this was probably caused by the redundant portion of the prolapsed aortic valve leaflet.

Another suggestive but not pathognomonic finding of this syndrome is the position of the aortic valve in the lateral view on selective thoracic aortography. The plane of the aortic valve is horizontal or tilted anteriorly, in contrast to that of the normal valve which is usually tilted posteriorly (Fig. 5).

LEFT VENTRICULOGRAPHY

Left ventriculography was performed in 3 cases. In 2 of the cases in which the aortic insufficiency was not marked, filling of the right ventricle through the ventricular septal defect could be demonstrated.

DISCUSSION

There is convincing evidence from the natural history of the syndrome, that the ventricular septal defect is the primary lesion and that the aortic insufficiency de-

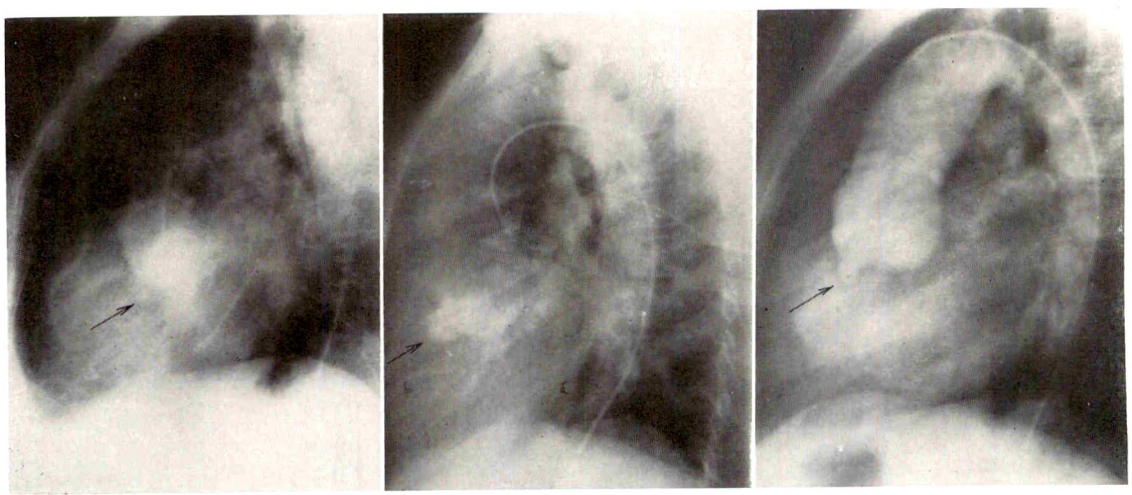


FIG. 6. Selective thoracic aortograms of various patients with prolapse of the posterior aortic cusp. A pocket-like extension is visualized below the involved cusp (arrow).

velops with the passage of time. This has been demonstrated by clinical, laboratory and pathologic data.[4,7,9,13,14]

It is not known why aortic insufficiency occurs in these cases. Several factors have been implicated;[9,12,14] these include the particular position of the ventricular septal defect, overriding of the aorta and displacement of the aortic leaflets downwards by the high velocity of blood through the ventricular septal defect; but there is sufficient evidence to refute all these theories.

The explanation for the existence of aortic insufficiency in these cases of ventricular septal defect possibly lies in the developmental patterns of the ventricular septum. It is known that the muscular portion of the septum has to move from left to right in its development and that the aorta shifts from right to left.[8] If these movements do not take place, the membranous septum is not continuous vertically with the muscular septum but an angle forms between them, and the membranous septum lies in a more horizontal plane than normally. In the ventricular septal defect produced by this failure of movement of the muscular septum, it can be assumed that the abnormal position of the membranous septum results in deficient support for the aortic valve cusps.

Roentgenographic examination may definitely aid in the diagnosis of the syndrome. Firstly, in the usual case of ventricular septal defect, the aorta is normal or even small in size. If, in a known or suspected case of ventricular septal defect, the aortic shadow is seen to become progressively enlarged and, particularly, if excessive pulsations are present on fluoroscopy, the diagnosis of aortic insufficiency due to and superimposed on the ventricular septal defect should be strongly suspected. Secondly, if in a case of ventricular septal defect serial roentgenograms reveal a progressive decrease in pulmonary vasculature, the two possibilities which should be considered are that the ventricular septal defect is undergoing spontaneous closure or that the production of aortic insufficiency and subsequent prolapse of the aortic cusps has caused partial or almost complete closure of the ventricular septal defect. In the latter case a parallel increase in the size of the aortic shadow will, of course, confirm the diagnosis.

From the practical standpoint, it is important to differentiate ventricular septal defect and aortic insufficiency from patent ductus arteriosus. In 10 per cent of the cases of ventricular septal defect and aortic insufficiency reported in the literature, patent ductus arteriosus was mistakenly diagnosed and the patients underwent exploratory thoracotomy.[12] It is not always possible to differentiate between these two conditions on auscultatory and phonocardiographic grounds. A roentgenologic clue may be provided by the size of the pulmonary artery which is dilated in cases of patent ductus arteriosus, whereas the pulmonary artery segment is not prominent and may have a normal appearance in cases of ventricular septal defect and aortic insufficiency. At fluoroscopy, heaving pulsations of the aorta are characteristic of aortic insufficiency and are usually less prominent in patent ductus arteriosus. In the latter cases excessive pulsations are present in the prominent pulmonary artery segment. The relative size of the left atrium and left ventricle may aid in the differential diagnosis. In cases of patent ductus arteriosus the left atrium and left ventricle are enlarged to the same degree, dependent on the shunt volume. In cases of ventricular septal defect with aortic insufficiency the left ventricular enlargement is usually the more prominent feature.

There are few reports on the diagnostic value of contrast roentgenography with regard to the diagnosis of ventricular septal defect and aortic insufficiency. Some authors used selective thoracic aortography and selective left ventriculography to evaluate the aortic insufficiency and to localize the ventricular septal defect.[9,11,14] Intravenous or selective right heart angiocardiography has been used for demonstration of the ventricular septal defect by

refilling of the right ventricle in the levo phase.[11] The importance of both selective right cardioangiography and selective thoracic aortography has not, however, been sufficiently stressed.

Obstruction in the region of the outflow tract of the right ventricle may be due to infundibular or valvular pulmonary stenosis, to a prolapsed aortic valve or to a combination of these lesions. Selective right heart cardioangiography may aid substantially in the differential diagnosis of these conditions.

The bulging sinus may occlude the ventricular septal defect when it descends and prolapses through the ventricular septal defect and a left-to-right shunt may, therefore, be missed during cardiac catheterization. This occurred in 1 of the cases of Garamella *et al.*[5] and in our case described above.

Some of the cases mentioned in the literature in which operations were performed had infundibular pulmonic stenosis, and resection of the infundibulum was necessary.[4,12] Nadas *et al.*[9] reported cases with pressure gradients between the right ventricle and pulmonary trunk, and yet these cases had little hypertrophy in the right ventricular infundibular region; they assumed that the prolapsing valve had caused the pressure gradient. The case described above presents angiographic evidence that such a prolapse may cause significant right outflow tract obstruction and may almost completely occlude the defect between the ventricles.

Selective thoracic aortography will demonstrate the presence of the aortic insufficiency and, in certain cases, the left-to-right shunt at the ventricular level may also be demonstrated. In those cases in which there is prolapse of the right aortic cusp, the characteristic step-like bulging of the right aortic sinus suggests the diagnosis of aortic insufficiency produced by the presence of a ventricular septal defect. Since the right sinus is involved in 75 per cent of the cases,[12] the importance of this sign is evident. In one of our cases a presumptive diagnosis of patent ductus arteriosus had been made. Selective thoracic aortography revealed the characteristic bulging of the right sinus with mild aortic insufficiency. In view of this finding, a diagnosis of aortic insufficiency of the type associated with ventricular septal defect was made and left ventriculography confirmed the diagnosis. Another characteristic sign was seen in 4 cases with prolapse of the posterior aortic cusp in which the redundant portion of the prolapsed cusp caused a pocket-like extension filled by contrast material below the involved cusp.

The early diagnosis of this syndrome is important because the cases with mild aortic insufficiency may be repaired by plastic correction of the aortic valve and closure of the ventricular septal defect. However, once the aortic insufficiency increases, aortic valve replacement becomes necessary.

SUMMARY

Ten cases of ventricular septal defect associated with aortic insufficiency are presented. In this syndrome the aortic insufficiency is a complication of the ventricular septal defect. The underlying anatomy is reviewed and a possible explanation for the presence of the aortic insufficiency is suggested.

The roentgenographic and cardioangiographic features are stressed. Thoracic aortography may reveal characteristic deformities produced by the involved aortic sinuses and their prolapsed leaflets. Selective right ventriculography may aid in the evaluation of the obstruction of the right ventricular outflow tract.

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PULMONARY REGURGITATION WITH VENTRICULAR SEPTAL DEFECT AND PULMONIC STENOSIS—TETRALOGY OF FALLOT VARIANT*

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CONGENITAL absence of the pulmonary valve with pulmonary regurgitation, as an isolated anomaly or in association with other intracardiac defects, is rare. Absence or near absence of the pulmonary valve is usually associated with a ventricular septal defect.[3,8,13,22,32]

In 1955, Rowe *et al.*[24] reported 4 cases of tetralogy of Fallot variants. In one instance there was absence of the pulmonary valve leaflets with pulmonary regurgitation. There are few other reports which relate the clinical and hemodynamic features of this unusual combination of anomalies. This report presents the clinical profile, hemodynamic and angiocardiographic features observed in 14 similar patients with absence of the pulmonary valve with pulmonary regurgitation, ventricular septal defect and pulmonic stenosis.

MATERIAL AND METHOD

From 1957 through 1966, 14 patients have been seen at Los Angeles Children's Hospital in whom a diagnosis of absence of the pulmonary valves with pulmonary regurgitation, ventricular septal defect, and pulmonary stenosis has been established. Postmortem examination was possible in 9 patients and definite anatomic diagnosis has been confirmed in 11. The diagnosis was established in the remaining 3 children on the basis of catheterization and angiocardiographic data. Fourteen cardiac catheterizations were performed on 12 of these patients. With one exception (Case 3) these studies were carried out under meperidine, promethazine, and chlorpromazine sedation and local anesthesia. Cardiac catheterization was performed by previously described methods.[26] Per cent of oxygen saturation was determined by a Cuvette oximeter. Blood flow data were based on assumed oxygen consumption estimations.[26] Pressure tracings were recorded through a strain gauge transducer and photo-oscillograph. Spot angiograms (7 cases), selective cineangiograms (2 cases) and bi-plane Elema roll film angiograms (3 cases) were obtained on 12 patients.

PATIENT MATERIAL

With the exception of one infant born to a mother with a "flu-like" illness during the third month of pregnancy, all 14 patients (9 females and 5 males) were born after an uncomplicated pregnancy and delivery. Birth weights ranged from 4 pounds 5 ounces to 8 pounds with a mean of 7 pounds. The mothers' ages ranged from 22 to 42 years, with a mean of 27 years. Two patients observed in this series were brother and sister. One patient was an identical twin. One had the clinical findings of Down's syndrome and another had had mild cerebral palsy.

The pertinent clinical data are shown in Table 1. Nine patients were noted to have mild to moderate cyanosis at rest and 5 patients had paroxysmal hypoxic spells in infancy. Two others gave a history of squatting. One infant (Case 9) who had repeated hypoxic spells, with disappearance of the murmur during the spell, had a severe prolonged pulmonary infection. During her hospital course, there was a question whether she may be in congestive failure. The observed hepatomegaly and pulmonary rales

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TABLE I

SUMMARY OF CASES

Case No.	Age when First Seen	Cyanosis	Spells	C.H.F.	Obstructive Respiratory Symptoms	Recurrent Respiratory Infections	Comment
1	1 yr.	+	−	−	−	−	Death—open heart surgery—9 years
2	2 yr.	−	−	−	+	+	Alive—open heart surgery—9 years
3	18 mo.	+	+	−	−	−	Death—catheterization—18 months
4	17 mo.	−	−	−	−	+	Death—open heart surgery—5 years
5	2½ yr.	−	−	−	−	+	Alive—unoperated—4 years
6	2 wk.	−	−	−	+	+	Death—Brock procedure—1 year
7	4 da.	+	−	−	+	+	Death—intercurrent infection—7 months
8	4 da.	+	−	−	−	+	Alive—open heart surgery—8 years
9	10 da.	+	+	+	+	+	Dead—hypoxic spell—3 months
10	6 wk.	+	+	−	−	−	Dead—hypoxic spell—6 weeks
11	2 mo.	−	−	+	−	+	Alive—unoperated—4 years
12	6 wk.	+	+	−	−	−	Dead—Brock procedure—5 years open heart surgery—7 years
13	1 yr.	+	−	−	−	+	Alive—unoperated—2 years
14	6 wk.	+	+	−	−	−	Death—Potts shunt—5 years
							Dead 9 Alive 5

C.H.F.—Congestive Heart Failure.
Spells—Hypoxic Spells.

were felt to be more related to respiratory failure and acidosis than to congestive heart failure. She presented the clinical problem of hypoxic spells in the presence of signs suggesting congestive heart failure. She was treated for congestive failure, pneumonitis and hypoxic spells without improvement. Two patients with a large left-to-right shunt were treated for congestive heart failure in infancy. Eight patients were relatively asymptomatic as regards their cardiovascular system, with the exception of mild dyspnea on exertion being noted in the older children.

Four patients had severe respiratory symptoms. Two (Cases 6 and 7) had right middle lobe emphysema secondary to compression by an aneurysmally dilated right pulmonary artery, which required right middle lobe lobectomies as infants on an emergency basis. The 2 other cases had recurrent atelectasis and pneumonia (Fig. 1). Five other patients gave a history of recurrent respiratory infections from infancy. Five patients had no pulmonary symptoms.

PHYSICAL EXAMINATION

Murmurs were noted at birth in 9 patients, and in 3 by the fourth neonatal day. In the remaining 2, the murmur was noted by 6 weeks of age. Each patient had a systolic thrill associated with a harsh systolic ejection murmur, heard maximally at the upper left sternal border. The second sound in the second to third left intercostal space was either diminished or inaudible. In each case, only a single component was identified (Fig. 2). Following the second

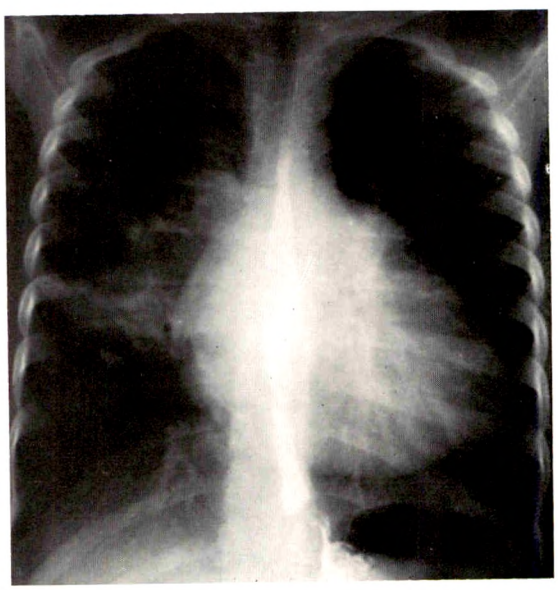


FIG. 1. Chest roentgenogram. Right middle lobe atelectasis secondary to compression by the aneurysmally dilated right pulmonary artery.

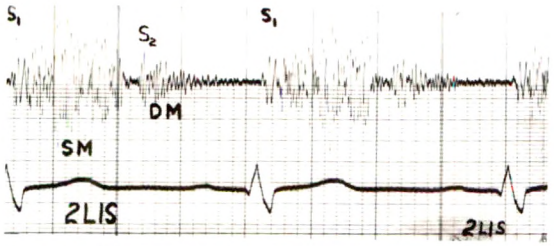


FIG. 2. Phonocardiogram (Case 2). The systolic ejection murmur (SM) ends before the single second sound (S_2). A medium-pitched decrescendic diastolic murmur (DM) follows the second sound.

sound, or systolic murmur, by a short but definite interval, was a medium-pitched, sometimes rough diastolic murmur which was heard best along the left sternal border from the second to the fourth left intercostal space. This was only occasionally accompanied by a thrill.

ELECTROCARDIOGRAMS

All electrocardiograms showed right ventricular hypertrophy as defined by standard electrocardiographic criteria.[18] The electrical axis varied from $+60°$ to $-165°$. No heart block, conduction disturbances, or left axis deviation were observed in these 14 patients. One patient with a large left-to-right shunt demonstrated at catheterization also had left ventricular hypertrophy.

CHEST ROENTGENOGRAMS

The chest roentgenograms demonstrated mild to moderate cardiac enlargement. The pulmonary vascularity was interpreted as normal to moderately increased in those cases with left-to-right shunts. Pulmonary vascularity was normal in those who had hypoxic spells. The most striking roentgenographic finding, however, was the enlargement of the main pulmonary artery and its immediate branches (Fig. 3). Aneurysmal dilatation of the pulmonary arteries may be recognized in the neonate roentgenogram, but this was not always evident in infants under 3 months of age. The dilated pulmonary arteries were sometimes obscured by a thymus shadow or were not readily identified. In infants over 3 months of age the prominent pulmonary arteries were always

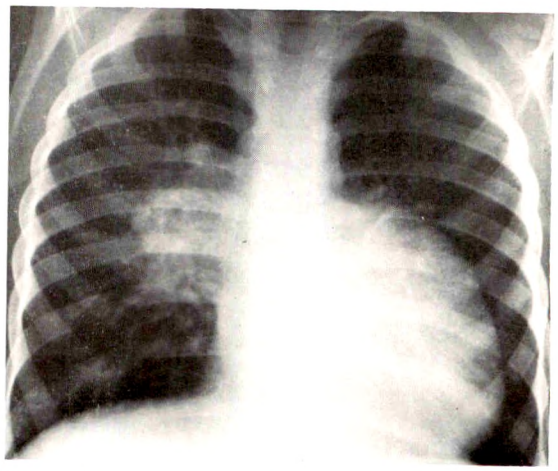


FIG. 3. Chest roentgenogram (Case 2). Mild cardiac enlargement is present. In the hilar area the dilated right and left pulmonary artery trunks are evident.

evident. In 11 of the 14 patients the prominence of the pulmonary artery segments was described as aneurysmal. Three patients' chest roentgenograms showed a prominent convexity at the upper left sternal border (Fig. 4). On serial observations, the aneurysmal changes of the pulmonary

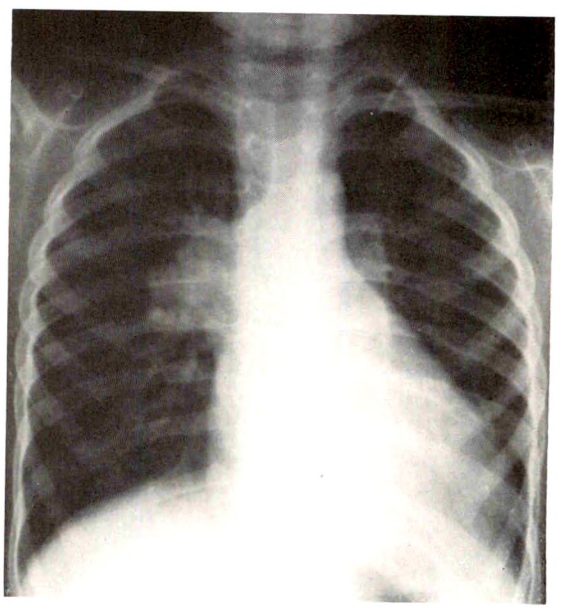


FIG. 4. Chest roentgenogram. The aneurysmally dilated right pulmonary artery is evident. The convexity at the upper left heart border corresponds to the dilated right ventricular infundibulum identified at angiography.

artery did not appear to be progressive. A right aortic arch was observed in 6 patients.

HEMODYNAMIC DATA

The catheterization findings are summarized in Table II: (a) Right-to-left shunting at the ventricular level alone was observed in 4 of 12 patients, and (b) solely left-to-right in 4; (c) bidirectional shunting at the ventricular level was present in 3 patients. One patient (Case 12) had a bidirectional shunt at the ventricular level at her first study, and only left-to-right at the second catheterization. The discrepancy in the two sets of oximetry data is related to the difficulties encountered during the first catheterization procedure. Right ventricular systolic pressures approximated systemic pressures in all cases. The pulmonary artery was entered in 9 cases and no pulmonary hypertension was recorded. The pressure tracings were not always characteristic of pulmonary regurgitation, nor was the pulmonary artery diastolic pressure equal to the right ventricular end diastolic pressure.[16] Absence of the dicrotic notch was not a consistent finding in the pulmonary arterial tracing.[27] The course of the catheter through the outflow area of the right ventricle into the pulmonary artery appeared to be normal except in 3 cases. In these 3 cases the catheter passed more laterally through the long infundibular outflow tract. This long infundibular tract corresponded to the convexity noted on the plain chest roentgenogram. Pullback tracings from the pulmonary artery to the right ventricle demonstrated pulmonary stenosis. The pressure tracings did not always delineate the site of obstruction as valvular of infundibular. Catheterization findings in all cases except one were compatible with a ventricular septal defect and pulmonic stenosis. In this case (Case 12) the data were interpreted as compatible with valvular pulmonic stenosis. In 4 earlier cases, absence or near absence of the pulmonary valve was not recognized.

Cineangiograms and biplane angiograms demonstrated sausage-like aneurysmal dilatation of the proximal pulmonary artery segments (Fig. 5) and some degree of pulmonary regurgitation. Right ventricular angiograms demonstrated infundibular stenosis. The 3 cases in which the course of the catheter was unusual demonstrated a

TABLE II

CATHETERIZATION DATA

Case No.	Age at Catheterization	O_2 Saturation (per cent)					Pressures*		
		SVC	RA	RV	PA	SA	RV	MPA	SA
1	1 yr.	67	68	65	—	83	92/.7	13/4 m=8	82/44
2	4½ yr.	56	57	55	68	92, 85	100/9	25/12	100/65
3	18 mo.	26	18	43	—	78, 66	70/3	—	79/38
4	3½ yr.	75	75	83	83	96	95/10	27/16	110/70
5	2 yr.	57	54	76	72	92	103/5	34/14	106/62
6	11 mo.	70	70	75	—	96	90/4	—	86/54
8	4½ yr.	59	62	74	78	85	95/2	32/17	100/50
9	3 wk.	73	73	75	78	86	80/6	24/10	70/40
11	1 yr.	69	69	78	80	94	95/8	20/8	90/60
12a	5 yr.	62	—	67	—	77	115/6	—	116/74
12b	7 yr.	69	79	85	83	93	86/10	20/9	110/70
13	1 yr.	44	48	48	—	73	84/0	—	90/52
14a	23 mo.	74	70	75	76	—	110/15	13/6	110/70
14b	5 yr.	65	70	65	—	85	98/13	23/13	112/83

SVC—Superior Vena Cava; RA—Right Atrium; RV—Right Ventricle; MPA—Main Pulmonary Artery; SA—Systemic Artery.
* Pressures in mm./Hg.

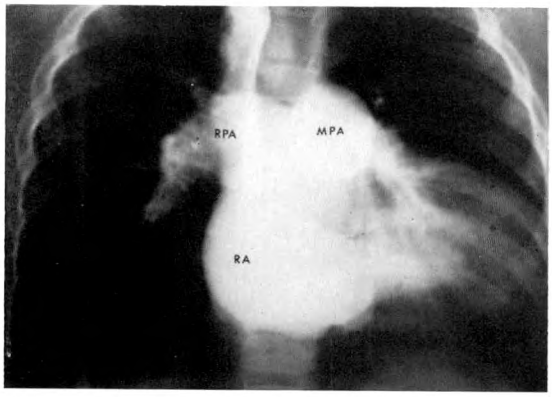


FIG. 5. Venous angiogram (frontal projection). There is opacification of the superior vena cava and right atrium (RA). The prominent main pulmonary artery (MPA) and sausage-like aneurysmal right pulmonary artery (RPA) are outlined.

dilated infundibulum[27] (Fig. 6, *A* and *B*), with minimal infundibular stenosis and a diminutive pulmonary valve annulus. Despite otherwise adequate angiograms, the pulmonary valves were not definitely visualized in 8 patients.

CLINICAL COURSE

Nine patients in this series died (Table 1). One death (Case 3) was related directly to cardiac catheterization, and another (Case 7) to an intercurrent infection. Two infants (Cases 9 and 10) died during hypoxic spells. Three patients died in the early postoperative period after having undergone correction of their intracardiac defects. These 3 patients' deaths (Cases 1, 4 and 12) occurred at the time of initial cardiopulmonary bypass surgery at this institution. Case 12 had a previous Brock valvulotomy procedure with a mistaken diagnosis of valvular pulmonic stenosis. No clinical improvement was noted after this surgery. Case 14 died during an attempted Potts anastomosis and Case 6 during an attempted Brock procedure at the age of 1

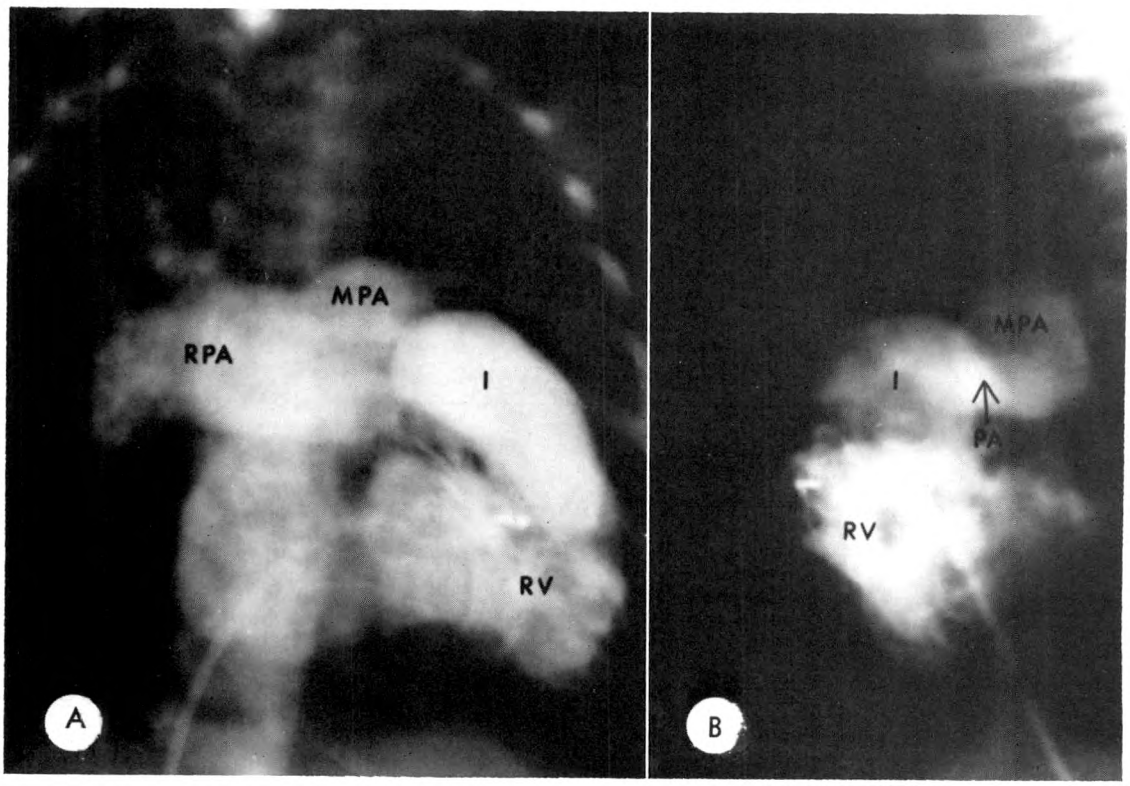


FIG. 6. (*A* and *B*) Right ventricular angiograms. Opaque material passes through the dilated infundibulum (I) into the main pulmonary artery (MPA) and aneurysmally dilated right pulmonary artery (RPA). The small pulmonary valve annulus (PA) is best seen in the lateral projection (arrow).

year. Five patients are alive and 2 have successfully undergone closure of their ventricular septal defect and resection of the infundibular pulmonic stenosis. Clinically, they are improved and have had no difficulties from pulmonary regurgitation. However, postoperative catheterization studies have not been performed.

PATHOLOGY

Nine specimens were available for examination. The weights of the hearts were heavier than of specimens of the control patients of comparable age and size without heart disease. In all cases, the right ventricle was greatly dilated and right ventricular hypertrophy was present. The right atrium was dilated. The circumference of the tricuspid ring was enlarged, but the tricuspid valve otherwise appeared normal. Seven specimens showed infundibular stenosis with a striking deficiency of the pulmonary valve cusp tissues (Fig. 7, *A* and *B*). In 2 cases, however, there was minimal obstruction in the infundibular area and the infundibulum was long and dilated. In these 2 cases there was marked narrowing of the pulmonary valve annulus. A moderate sized ventricular septal defect in the usual location as seen in tetralogy of Fallot was present. One specimen demonstrated a double outlet right ventricle.[21] Six of nine cases had right aortic arches. Two had a retro-esophageal right subclavian artery and 1 had a retro-esophageal left subclavian artery.

The pulmonary valve was represented either by absence of demonstrable valve tissue or puckered fibrous valvular tissue. Characteristically the main pulmonary artery, and to a lesser degree, the left and right branches of the main pulmonary artery, were so aneurysmally dilated that the aorta appeared to be diminished in size.

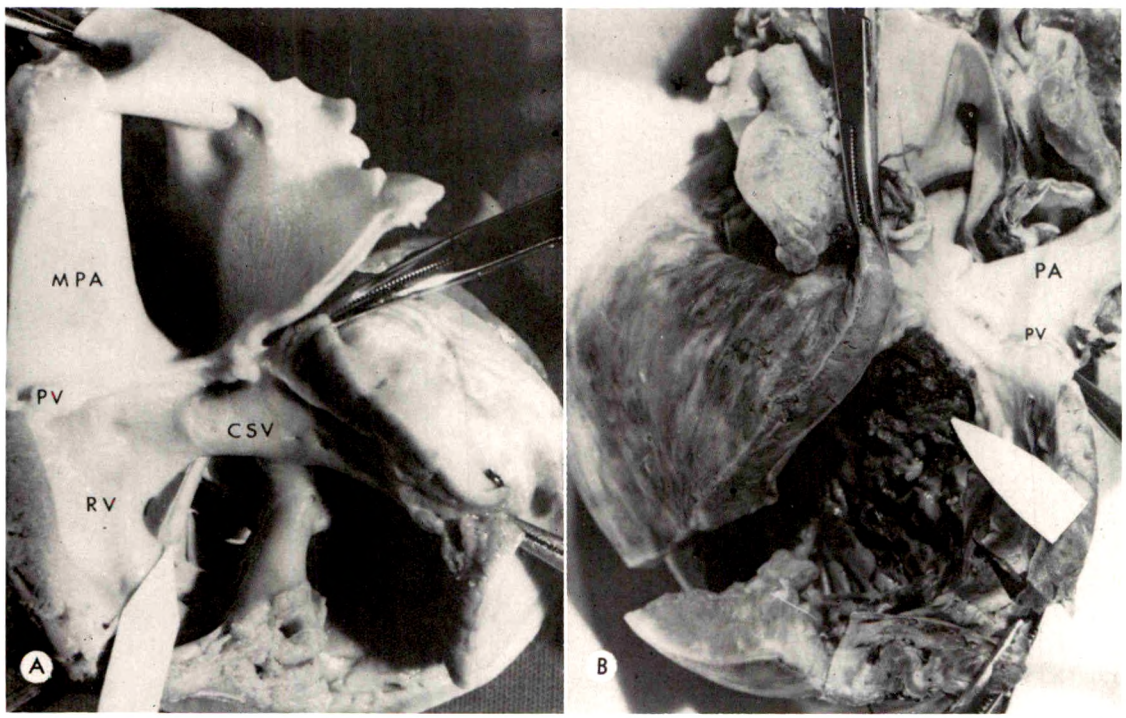


Fig. 7. (*A*) The right ventricle (RV) is enlarged and the crista supraventricularis (CSV) is prominent. No demonstrable pulmonary valve tissue is present at the pulmonary valve annulus (PV). The main pulmonary artery (MPA) is aneurysmally dilated. (*B*) The arrow points to the area of extensive infundibulectomy. The pulmonary valve annulus (PV) is represented by nubbins of puckered fibrous ridges. The pulmonary artery (PA) segment is dilated.

One specimen had absence of the left pulmonary artery (Case 14).[19] Total wall thickness of the pulmonary artery showed no significant difference when compared with normal controls.[28] Previous reports have shown changes in the elastic tissue of the main pulmonary artery.[16]

DISCUSSION

Congenital absence or near absence of the pulmonary valve with pulmonary regurgitation is uncommon and the incidence of this anomaly is unknown. Some 30 cases have been reported in the literature.[6,27] Absence of the pulmonary valve can occur as an isolated lesion.[5] While this lesion may be associated with severe failure in infancy,[12,30] long term survival has been recorded.[23]

Most often this anomaly has been associated with a ventricular septal defect. The consequences of a large ventricular septal defect, pulmonary hypertension, and absence of the pulmonary valve have been cited previously.[3,8,22,29,32,33] Many have ventricular septal defects and infundibular pulmonic stenosis and have been termed tetralogy of Fallot variants.[10,15,16,20,24,27]

In these cases the anatomic findings are those of tetralogy of Fallot in addition to the aneurysmal dilatation of the pulmonary trunks and absence or near absence of the pulmonary valve. All 9 autopsy cases demonstrated infundibular stenosis[31] as expected. Two autopsy cases, however, demonstrated minimal infundibular obstruction. In these 2 instances, the major obstruction seemed to be at the pulmonary valve annulus. The pulmonary valve annulus circumference is usually less than that observed for the aortic valve[14] in tetralogy of Fallot. The valve circumferences in our cases were compared with standard norms.[7,14,25] In 5 of 9 cases the aortic valve circumferences were greater than the maximum value for that age group and in 2 were equal to the mean value. However, in 3 cases the aortic valve circumferences were slightly less than the minimal value for control standards. By contrast the pulmonary valve annulus circumferences except in 1 case were less than the minimum value for the standard controls.

Landing and Hughes,[14] and de la Cruz *et al.*[7] demonstrated a wide range of valve circumferences in normal children, which precludes the simple use of valve circumference measurements as rigid criteria for the diagnosis of functional stenosis or incompetence. Landing and Hughes[14] correlated pulmonary valve/aortic valve ratios and showed a decreased pulmonary valve/aortic valve ratio in tetralogy of Fallot and pulmonic stenosis. In our series the pulmonary valve ratio was less than the 1.1 anticipated for normal controls and ranged from 0.3 to 0.9. Five were in the lowest one percentile range of the control group. This included the 2 cases who appeared to have minimal infundibular obstruction. In 2 cases the pulmonary valve/aortic valve ratio was less than 0.5. One patient (Case 4) died after open heart surgery and the other died in infancy (Case 5). In these 2 cases the pulmonary obstruction was predominantly located at the pulmonary valve annulus.[14]

The association of the pulmonary artery dilatation with absence or near absence of the pulmonary valve is constant. The pathogenesis of the dilated pulmonary artery is unknown. Whether this is secondary to a muscular abnormality at the base of the pulmonary artery,[3] related to an intrinsic abnormality of the elastic tissue of the pulmonary artery, or in part secondary to the hemodynamics of the intracardiac anomalies is an unsettled question. Other anomalies, such as complete endocardial cushion defect,[6,33] patent ductus arteriosus,[33] hypoplastic left heart,[33] double outlet right ventricle,[1,6,33] and Marfan's syndrome[4] have been reported with absence or near absence of the pulmonary valve.

The etiology of this lesion is unknown. The fact that one mother had a "flu-like" illness in early pregnancy raises a question of a possible viral etiology. However, 2 children were from the same family, which suggests a genetic factor. One patient had the characteristics of Down's syndrome

and another was an identical twin. In our series this lesion was more common in females—an observation that had not previously been reported.[6,27]

Pulmonary regurgitation with absence or near absence of the pulmonary valve with ventricular septal defect and pulmonic stenosis presents a typical clinical profile. The presence of a harsh systolic murmur, with a characteristic diastolic murmur occurring at a definite interval after the aortic closure in association with right ventricular hypertrophy and roentgenographic findings of marked dilatation of the main pulmonary artery, with or without a right aortic arch, makes clinical recognition possible. Differential diagnosis in our patients included a coronary arteriovenous fistula, ventricular septal defect with aortic insufficiency, tetralogy of Fallot with patent ductus arteriosus, truncus arteriosus, and ruptured sinus of Valsalva. In the last 6 cases, the diagnosis was recognized prior to catheterization.

Definite anatomic diagnosis can be established by cardiac catheterization and angiocardiography. Right ventricular angiocardiography will outline the abnormalities of the pulmonary arteries and suggest absence or near absence of the pulmonary valve. Left ventricular and aortic angiocardiography should be performed to rule out the presence of an endocardial cushion defect, double outlet right ventricle, and aortic insufficiency. Because of incomplete studies, 4 earlier cases were not recognized as having absence or near absence of the pulmonary valves and were called isolated tetralogy of Fallot syndrome or pulmonary valve stenosis. These errors in preoperative diagnosis contributed directly to operative mortality in 3.

The hemodynamic spectrum of our patients ranged from tetralogy of Fallot physiology with hypoxic spells[11,17] in 5 cases to that of a large left-to-right shunt with congestive heart failure in 2. Four of 14 patients also had severe respiratory symptoms in infancy, secondary to obstruction from the aneurysmal dilatation of the right pulmonary artery, which in 2 cases necessitated emergency lobectomies because of right middle lobe emphysema. Two patients had recurrent episodes of right middle lobe atelectasis and pneumonia, which necessitated multiple hospitalizations during infancy. They had less difficulties from pulmonary complications after 1 year of age. Obstructive symptoms from compression by either the left[6,16] or right[16] pulmonary arteries have been reported. Our pathologic data did not indicate any other obstruction secondary to the dilated pulmonary arteries (*e.g.*, pulmonary veins). Seven patients gave histories of recurrent respiratory infections and bronchitis in infancy and childhood, but these were not progressive and were not associated with obstructive emphysema or atelectasis. The direct association of these infections to the dilated pulmonary arteries is not known. Pulmonary function studies were not carried out on these older children to ascertain any intrinsic abnormalities of their pulmonary system. D'Cruz *et al.*[6] have suggested that progressive symptoms in early childhood are unlikely, even in the presence of dilated pulmonary arteries, because of the stability of the tracheobronchial tree to resist extramural pressures. There was no correlation between hypoxic spells and the severity of the respiratory symptoms, but there was correlation with the severity of the outflow obstruction, as expected.

The management of these patients is the same as that followed in the usual case with ventricular septal defect with infundibular stenosis. Two infants with congestive heart failure were stabilized by usual medical management. Five patients had histories of hypoxic spells that would have necessitated some type of palliative surgery under 1 year of age. Even though this group of patients can well have both cardiac and respiratory difficulties, only 4 deaths were reported under 1 year of age. Two deaths were related to hypoxic spells, 1 directly to an intercurrent pulmonary infection, and 1 to surgery.

Which palliative procedure would be best for those who have hypoxic spells is debatable. A Brock procedure (infundib-

ular resection)[9] theoretically would be the treatment choice in those cases where there is infundibular obstruction of a significant degree. In our hands this approach has not been successful. Because of the size of the pulmonary arteries and apparent abnormalities of the vessel walls, a systemic pulmonary artery shunt procedure may cause further dilatation of the pulmonary arteries. However, a shunt procedure will be necessary for those symptomatic infants who have minimal outflow obstruction and a very narrow pulmonary valve annulus. Open heart correction of the intracardiac defects should be delayed as long as possible. Total correction, with closure of the ventricular septal defect and relief of the right ventricular outflow obstruction, can be carried out successfully, but with a more significant mortality than encountered in the usual tetralogy of Fallot case. Ideally, total correction should include placement of a homograft valve at the pulmonary annulus.[34] Total correction with a homograft valve placement in this tetralogy of Fallot variant has been reported.[34]

SUMMARY

Fourteen cases of ventricular septal defect with infundibular pulmonic stenosis and absence or near absence of the pulmonary valve are reported.

The presence of typical murmurs and typical roentgenograms makes the clinical diagnosis of this entity possible. Definite diagnosis of this tetralogy of Fallot variant can be established by catheterization and angiocardiographic procedures.

The problems of management of this tetralogy of Fallot variant are discussed.

The association of respiratory tract symptoms is emphasized.

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URINARY TRACT ANOMALIES IN CHILDREN WITH CONGENITAL HEART DISEASE*

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THE purpose of this report is to emphasize the importance of, and to demonstrate the significance of, obtaining a routine postangiographic abdominal roentgenogram or abdominal cineradiograph in infants and children undergoing angiographic examinations for congenital cardiovascular disease, as a screening technique for the detection of urinary tract anomalies. In addition, the incidence and nature of urinary tract anomalies associated with congenital heart disease can be determined. Humphry and Munn,[6] in a series of 450 patients, found satisfactory visualization of the urinary tract in 89 per cent of the cases by obtaining a single postangiographic abdominal roentgenogram.

Since the treatment of patients with congenital heart disease usually involves a major surgical procedure, it is of considerable importance to know when concomitant congenital renal lesions exist. Surgical correction of obstructive uropathy may be necessary before surgical correction of congenital heart disease can be safely performed. With renal cine and/or roentgenographic screening, urinary tract anomalies can be discovered and treated prior to the onset of symptoms which may occur only after extensive renal damage has resulted from prolonged obstructive uropathy.

It has been our practice to briefly fluoroscope the abdomen after completing cardiac catheterization and cineangiocardiography and to obtain a scout roentgenogram. If the urinary tract is not well visualized or if any abnormality is noted, a roentgenogram of the abdomen is obtained. When a urinary tract abnormality is confirmed, intravenous pyelography is performed. During an 18 month period, 179 cardiac catheterization and angiographic procedures were performed on pediatric patients. During this interval, 7 patients (3.9 per cent) were found to have urologic abnormalities, of which 5 were previously undetected.

REPORT OF CASES

CASE I. This male infant was a product of a normal full-term pregnancy and spontaneous delivery. Jaundice was present in the neonatal period. Bilateral cryptorchidism was noted. The baby failed to thrive, was listless and had frequent respiratory infections. A murmur was first heard at 16 days of age. The baby was digitalized at 5 months of age, but failed to improve. At 6 months of age he weighed 12 pounds (below third percentile). Cardiac catheterization and cineangiocardiography were done. The findings were those of a mild pulmonary valvular stenosis (right ventricular pressure 50/8, pulmonary artery pressure 25/10) with defective pulmonary valve and pulmonary valvular insufficiency. Abdominal cineradiography was performed and a roentgenogram of the abdomen was obtained immediately following the cineangiography. Bilateral hydronephrosis due to ureteropelvic obstruction was noted (Fig. 1). A left ureteroplasty was performed, and at a later date the procedure was repeated on the right side. When last seen at the age of 19 months, the baby weighed 21 pounds and was in the third percentile for weight and appeared robust and asymptomatic.

Although failure to thrive was attributed to congenital heart disease and frequent respiratory infection, the cardiac lesion was not severe. A urologic abnormality was unsuspected prior to the cardiac catheterization procedure and the child improved remarkably following surgical correction of the bilateral hydronephrosis.

CASE II. This male infant was initially seen at 8 weeks of age at which time a murmur was first heard. He was dehydrated and cachectic

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after being treated for diarrhea. Cardiac catheterization was performed, which confirmed a clinical diagnosis of patent ductus arteriosus and ventricular septal defect. Immediately following cineangiography, fluoroscopy of the abdomen revealed marked dilatation of the renal pelvis with prompt opacification on the right and delayed opacification on the left (Fig. 2, *A* and *B*). A very large bladder was noted. A subsequent cystogram showed bilateral reflux. The urinary tract was decompressed with a Foley catheter. The ductus arteriosus was divided. Later, supravesical urinary diversion was performed.

Case III. This male infant was followed from infancy after a murmur was first detected. He developed normally without cardiac or urologic symptoms. Cardiac catheterization was performed at 5 years of age. The findings were those of a ventricular septal defect with infundibular pulmonary stenosis (acyanotic tetralogy of Fallot). Bilateral hydronephrosis was noted on abdominal fluoroscopy immediately following the catheterization procedure. The subsequent intravenous pyelogram is shown in Figure 3. Cystography was performed and showed no reflux. As yet, no corrective surgery has been carried out. A recent intravenous pyelogram has shown improved drainage bilaterally.

Case IV. This 16 year old boy was known to have a heart murmur since childhood. He had symptoms of fatigue and cyanosis with exertion. No urinary symptoms were present. A diagnosis of ventricular septal defect with valvular pulmonary stenosis was made at the time of catheterization. Subsequent renal fluoroscopy showed a large left kidney with no visualization of the right kidney (Fig. 4). Subsequent studies confirmed a diagnosis of aplasia of the right kidney. The patient refused cardiac surgery.

Case V. This 7 month old male was noted to have a single umbilical artery at birth and a diagnosis of congenital heart disease was made shortly after birth. This was confirmed by cardiac catheterization and cineangiocardiography elsewhere, at which time nonfunction of the left kidney was found. Repeat cardiac catheterization and angiocardiography revealed ventricular septal defect with mild infundibular pulmonary stenosis. The subsequent abdominal



Fig. 1. Case I. Bilateral hydronephrosis due to ureteropelvic obstruction.

cine study and roentgenograms showed nonfunction of the left kidney.

Case VI. During the second day of life this female infant became cyanotic and developed a murmur. The infant had a deformed, low set left ear and a deformity of the left thumb with an absent metacarpal. The baby improved following oxygen and thereafter did quite well, although cyanosis remained. Cardiac catheterization and angiography were performed at 6 days of age. The findings were those of tetralogy of Fallot and right-sided aortic arch. Abdominal cine study showed hydronephrosis of the right kidney and the left kidney was not identified. A subsequent intravenous pyelogram demonstrated hydronephrosis of the right kidney and a poorly functioning ectopic left kidney with hydronephrosis which was thought to be due to obstruction at the ureteropelvic junction (Fig. 5, *A* and *B*). A cystourethrogram was negative. The patient is awaiting pyeloplasty.

Case VII. This 12 year old girl had a murmur

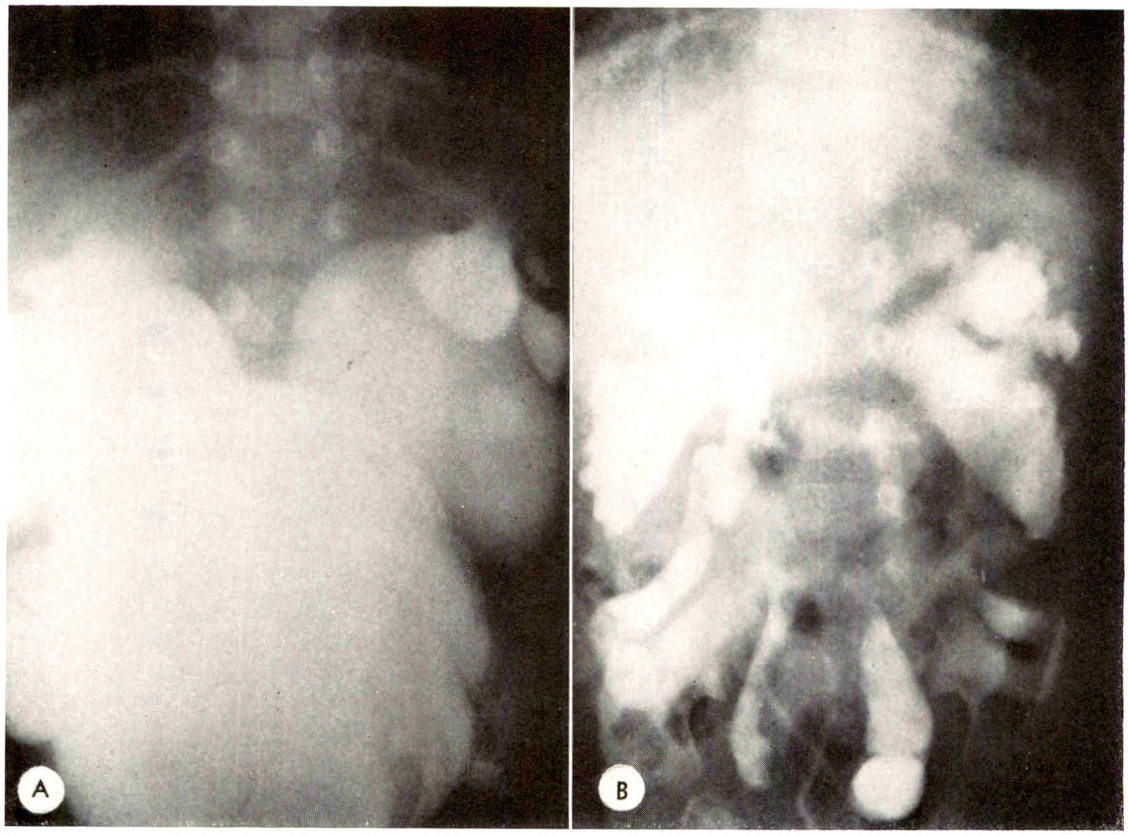


FIG. 2. Case II. Primary urethral obstruction with secondary ureterovesical obstruction. (*A*) Bilateral dilatation of the renal pelvis with dilated bladder. (*B*) Urogram obtained after bladder catheterization. Marked dilatation and tortuosity of the ureters are evident.

since infancy with a history of 2 urinary tract infections in early childhood. An intravenous pyelogram in early childhood demonstrated a duplicated ureter on the left. Cardiac catheterization and cineangiocardiography confirmed the clinical diagnosis of moderate pulmonary stenosis. The abdominal cine study showed a duplicated ureter on the left. Pulmonary valvulotomy was subsequently performed with excellent results.

DISCUSSION

Of the 7 cases in this report, in 2 the urinary tract anomalies were previously known to be present. In Case V, a nonfunctioning left kidney was demonstrated by the same method in the newborn period elsewhere. In Case VII, a previous intravenous pyelography had been done because of urinary tract infection. Urinalysis was normal in 6 cases at the time of study. In Case II, the specific gravity was persistently low. The blood urea nitrogen was normal in all cases at the time of study. Urinary tract evaluation was indicated in Cases V and VI; the former because of the presence of a single umbilical artery and the latter because of the low set deformed ear, since renal anomalies are occasionally associated with the former[2] and frequently present with the latter[9] anomaly. Early detection of obstructive uropathy in Case I and Case II permitted early corrective urologic surgery, preventing renal damage in the first patient. Surgery is planned for Case VI. The cases are listed in Table I.

The true incidence of urogenital anomalies in the general population is not known. McIntosh *et al.*[7] recorded a malformation incidence of 0.7 per cent in children surviving more than 1 month. However, all

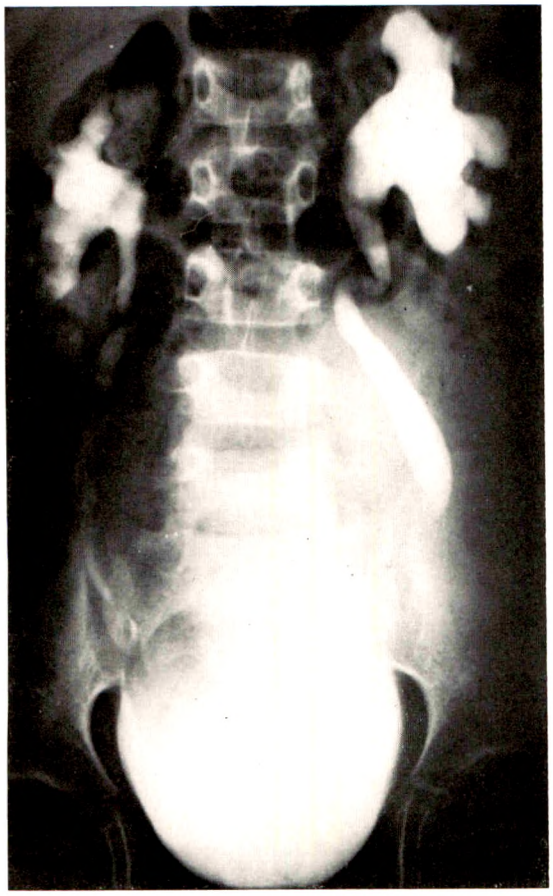


FIG. 3. Case III. Bilateral hydronephrosis; ureterovesical obstruction.

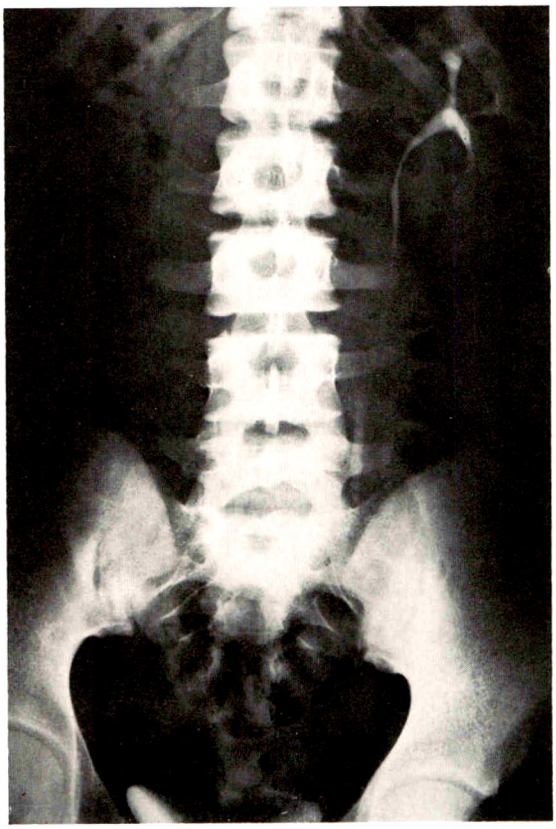


FIG. 4. Case IV. Agenesis of the right kidney. The left kidney is larger than normal.

TABLE I

SUMMARY OF CASES

Case No.	Age	Sex	Cardiac Abnormality	Urinary Abnormality	Associated Findings
I	6 mo.	M	Pulmonary valvular stenosis and insufficiency	Bilateral hydronephrosis due to ureteropelvic obstruction	Bilateral cryptorchidism
II	8 wk.	M	Patent ductus arteriosus and ventricular septal defect	Bilateral hydronephrosis due to ureterovesical obstruction	
III	5 yr.	M	Acyanotic tetralogy of Fallot	Bilateral hydronephrosis	
IV	16 yr.	M	Pulmonary valvular stenosis and ventricular septal defect	Aplasia of left kidney	
V	7 mo.	M	Mild infundibular stenosis and ventricular septal defect	Aplasia of left kidney	Single umbilical artery
VI	6 da.	F	Tetralogy of Fallot and right-sided aortic arch	Bilateral hydronephrosis due to obstruction at ureterovesical junction	Absent metacarpal, deformed left ear
VII	12 yr.	M	Moderate pulmonary valvular stenosis	Duplicated left ureter	Repeated urinary infections

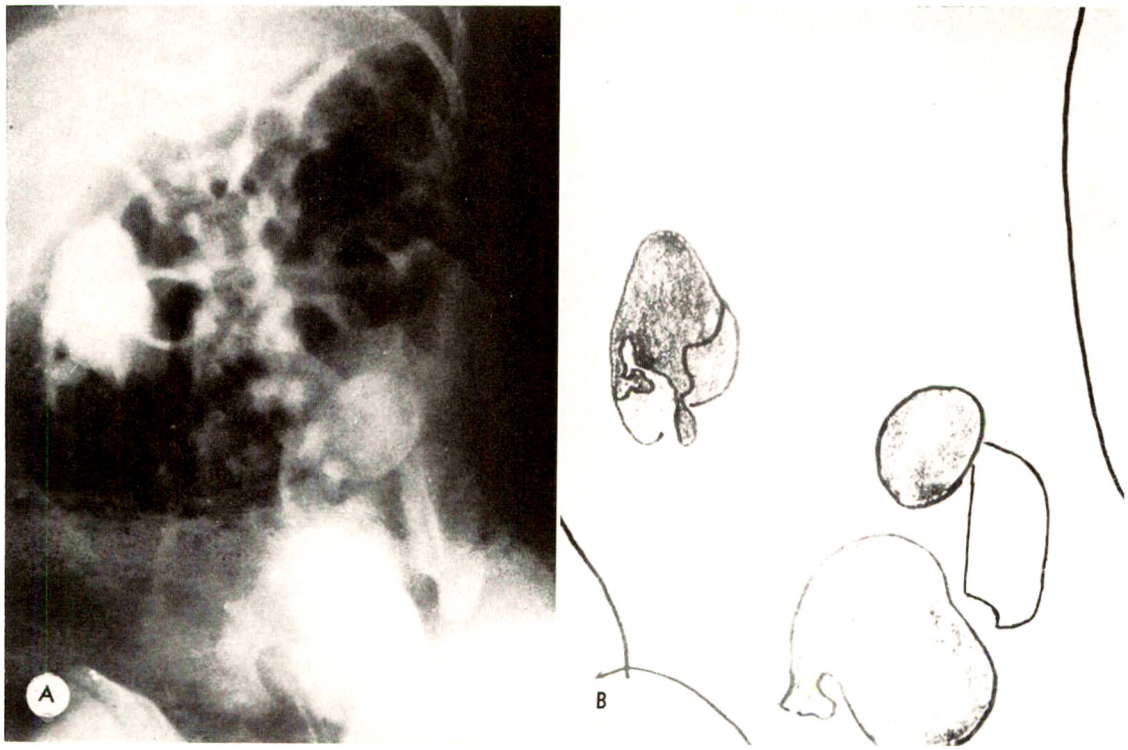


FIG. 5. Case VI. (*A*) Bilateral hydronephrosis with poorly functioning ectopic left kidney. (*B*) Outline of the renal pelvis and bladder. The ureters are not identified.

but 3 of the 41 anomalies discovered were hypospadias, undescended testicle and hydrocele. Other urinary tract anomalies may not have been manifest when the study was done, and no attempt was made to discover them in the asymptomatic subjects.

Felton[3] perhaps came closest to determining the incidence of upper urinary tract anomalies when he reviewed the autopsy reports of 152 children dying of causes other than urinary tract involvement and found an incidence of 2 per cent. However, many urogenital malformations remain undiagnosed, even at autopsy. Campbell[1] reported an incidence of 1:161 from an autopsy series of 51,880 cases and Nation[8] found an incidence of 109 cases of ureteral duplication in 16,000 autopsies. Hipona and Melnick[5] reported the findings of postangiographic abdominal roentgenograms in 1,233 patients and detected 12 congenital urinary tract abnormalities in 493 patients with congenital heart disease. Humphry and Munn,[6] by postangiographic abdominal roentgenograms, found 22 urinary tract abnormalities in 400 patients with congenital heart disease, of which 9 were serious abnormalities. There was no constant relationship between the type of cardiac anomaly and the type of urinary tract anomaly. These findings, with ours, are presented in Table II.

CONCLUSION

The urinary tracts of 179 pediatric patients with congenital cardiac disease have been studied with the routine use of abdominal cineradiographs or roentgenograms following angiography.

Seven of these patients (3.9 per cent) were found to have significant renal disease. This incidence appears to be somewhat higher than in the general population without cardiac malformations.

Unsuspected renal disease has been discovered by this means and is tabularly

TABLE II

URINARY TRACT DISEASE DEMONSTRATED BY POSTANGIOGRAPHIC PYELOGRAM OR ABDOMINAL ROENTGENOGRAM

Author	Hipona and Melnick[5] (New Haven)	Humphry and Munn[6] (Toronto)	Good Samaritan Hospital (Phoenix)
Cases studied	493	400	179
Agenesis	3	2	2
Hypoplasia	1		
Horseshoe kidneys	3	4	
Retrocaval ureter	2		
Vesical diverticulum	1		
Ectopic kidney	1	5	
Hydronephrosis	1	4	4
Rotated kidney		3	
Duplicated ureter		4	1
Total abnormalities	12 (2.4%)	22 (5.5%)	7 (3.9%)

compiled. Accompanying roentgenograms are shown.

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CONGENITAL ABSENCE OF THE PULMONARY VALVE: REPORT OF EIGHT CASES WITH REVIEW OF THE LITERATURE*

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ABSENCE of the pulmonary valve cusps is a rare congenital cardiac malformation. It is usually associated with tetralogy of Fallot but occasionally occurs with ventricular septal defect. Absence of the pulmonary valve without other cardiac abnormalities has been observed in only 4 of the 40 patients reported with this malformation.

This paper records the clinical and roentgenologic findings in 8 infants with absent pulmonary valve leaflets and reviews the literature on this condition. It also stresses the respiratory complications secondary to aneurysmal dilatation of the pulmonary artery. Six infants had tetralogy of Fallot and 1 had the Eisenmenger complex; 1 had no other cardiac malformation.

REPORT OF CASES

CASE I. M.S., a cyanotic white girl 2 days of age, was admitted to Children's Hospital of Pittsburgh on December 11, 1967. On physical examination a thrill was felt over the precordium and a Grade 4–6 to-and-fro harsh blowing murmur was heard over the lower left sternal border. P2 was not heard.

Electrocardiography revealed balanced axis with right ventricular hypertrophy.

Roentgenogram of the chest (Fig. 1*A*) showed cardiomegaly and a huge right pulmonary artery. The right upper and lower lobes were emphysematous; the right middle lobe was atelectatic.

Cineangiocardiography (Fig. 1, *B* and *C*) showed marked dilatation of the main and right pulmonary arteries and moderate dilatation of the left, ventricular septal defect, and pulmonary stenosis. Tracheobronchograms (Fig. 1, *D* and *E*) disclosed compression of the trachea and right main stem bronchus by the enlarged right pulmonary artery.

Because the infant developed severe respiratory distress after bronchoscopy, aneurysmorrhaphy of the right pulmonary artery was done. She died 2 days later.

At necropsy the cusps of the pulmonary valve were absent (Fig. 1*F*) and its ring was stenosed. The pulmonary artery and its right branch were markedly dilated. The left pulmonary artery was moderately dilated. The right auricle was large and the foramen ovale was patent. The right ventricle was thick-walled and dilated. A large membranous ventricular septal defect was present. The left superior vena cava opened into the coronary sinus. The wall of the dilated pulmonary artery was histologically normal.

CASE II. T.M., a $2\frac{1}{2}$ month old white girl was admitted to Children's Hospital of Pittsburgh on October 7, 1958 because of intermittent

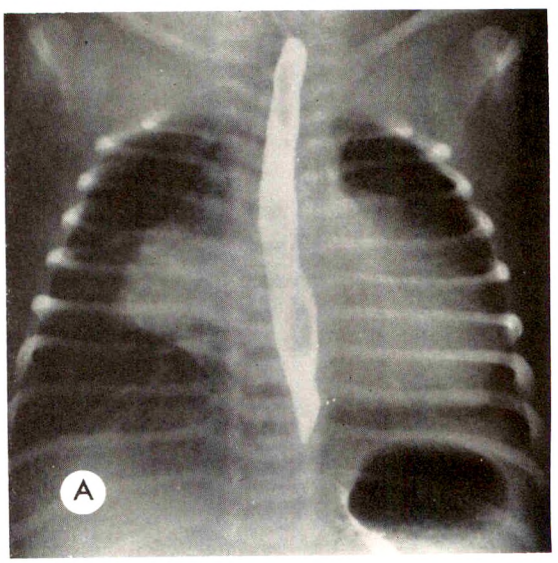


FIG. 1. Case 1. (*A*) Frontal roentgenogram of the chest. The heart is enlarged as is the right pulmonary artery. The right upper and lower lobes are emphysematous and the right middle lobe is atelectatic.

* From the Departments of Radiology and Cardiology, Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania and the University of Pittsburgh School of Medicine.

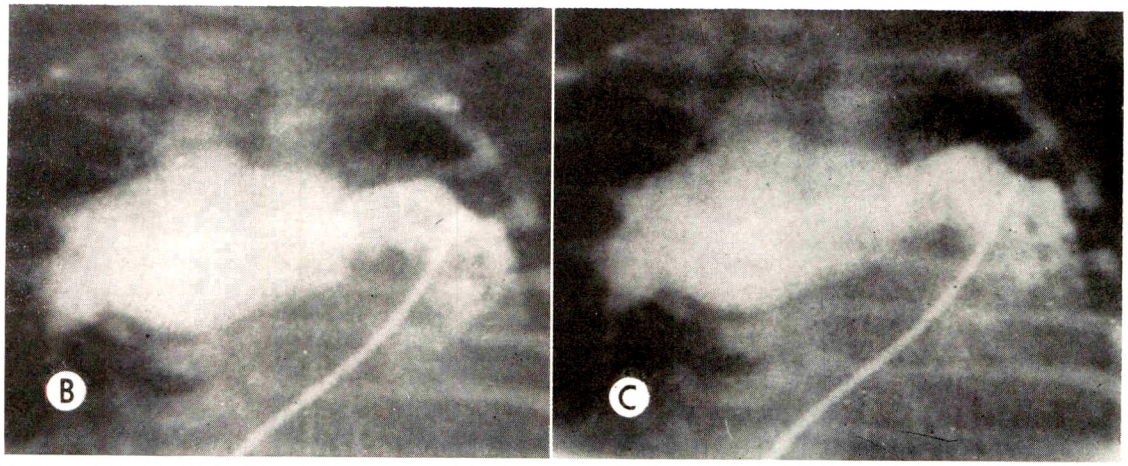


FIG. 1. (*B* and *C*) In the cine films the main, right and left pulmonary arteries are dilated.

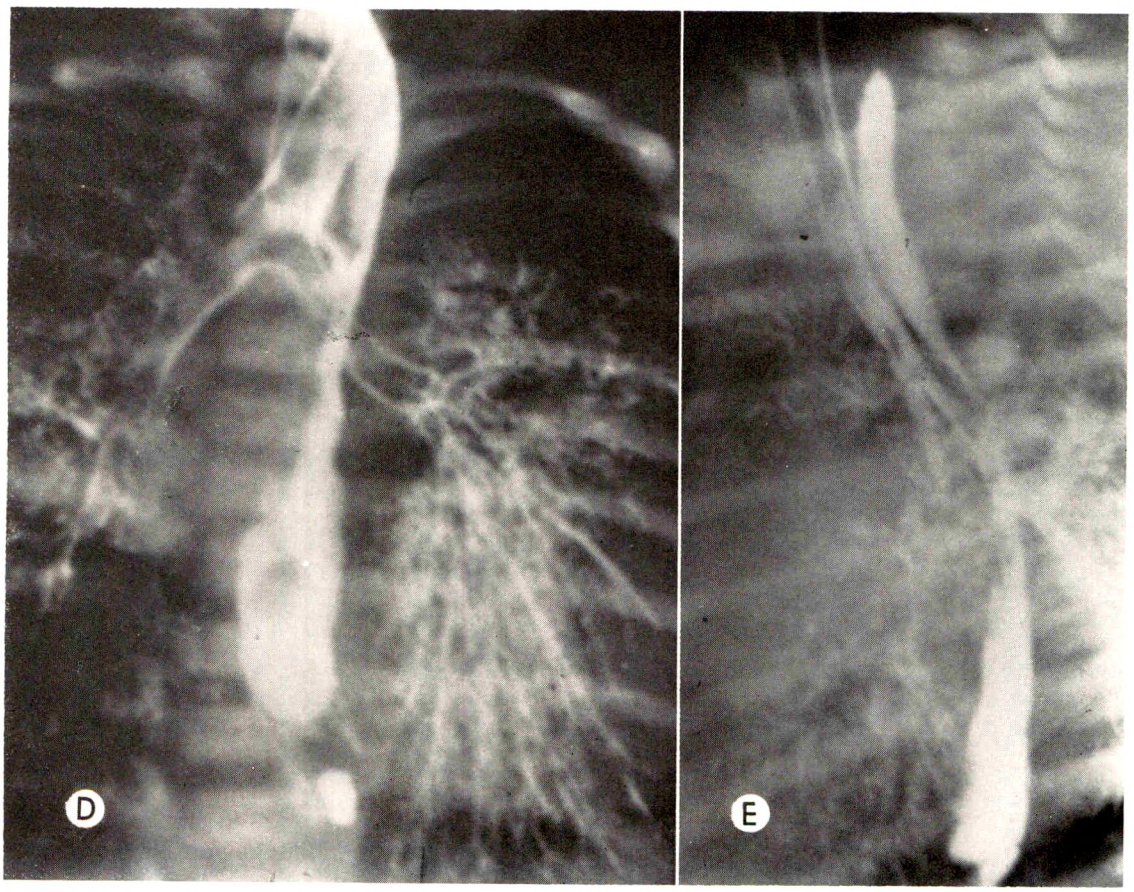


FIG. 1. (*D* and *E*) Tracheobronchograms. The trachea and right main stem bronchus are compressed by the enlarged right pulmonary artery.

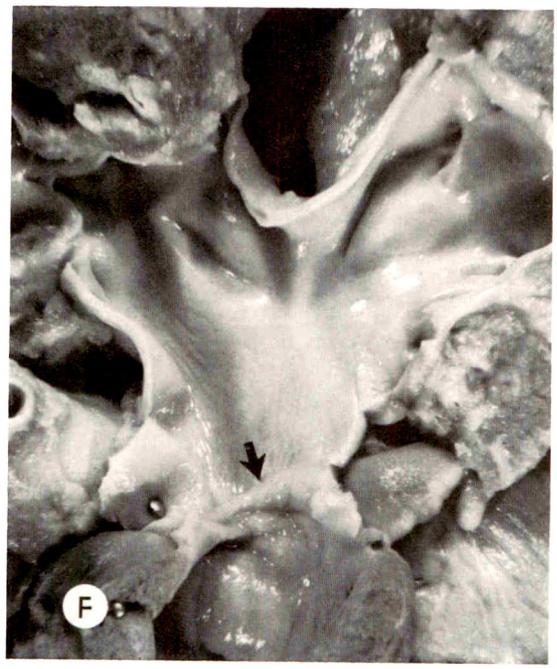


FIG. 1. (*F*) Postmortem specimen of the heart. The pulmonary arteries are dilated; the pulmonary valvular ring is stenosed; its leaflets are absent (arrow).

cyanosis and wheezing since birth. She was slightly cyanotic at rest and became more cyanotic when she cried. On physical examination, expiration was prolonged and respiratory wheezes were heard over the entire chest. A systolic thrill was palpable over the precordium. A loud, harsh systolic murmur and a Grade 1 diastolic murmur were heard at the lower left sternal border. The second pulmonary sound was diminished.

Electrocardiography showed balanced axis with sinus rhythm.

Roentgenogram of the chest (Fig. 2*A*) demonstrated moderate cardiomegaly, overaerated lungs, and a rounded mass of water density in the posterior superior portion of the mediastinum on the left. The peripheral vascular markings on the left were conspicuously diminished. At bronchoscopy the mass pulsated and compressed the trachea.

Retrograde aortogram and venous angiogram (Fig. 2*B*) showed marked dilatation of the pulmonary artery and its main branches, ventricular septal defect, pulmonary stenosis, and patent foramen ovale. The aorta was left-sided. The infant died 12 hours after angiography.

At necropsy the dilated pulmonary artery compressed the trachea and right main stem bronchus. The right lung was overaerated. There were absent pulmonary valve cusps, ventricular septal defect, subvalvular pulmonic stenosis, hypertrophy of the right ventricle, and probe-patent foramen ovale. The wall of the pulmonary artery was not examined microscopically.

CASE III. E.O., a 2 month old white boy, was admitted to Children's Hospital of Pittsburgh on November 2, 1961 because of heavy breathing since birth. He developed perioral cyanosis and his hands turned blue when he cried. Physi-

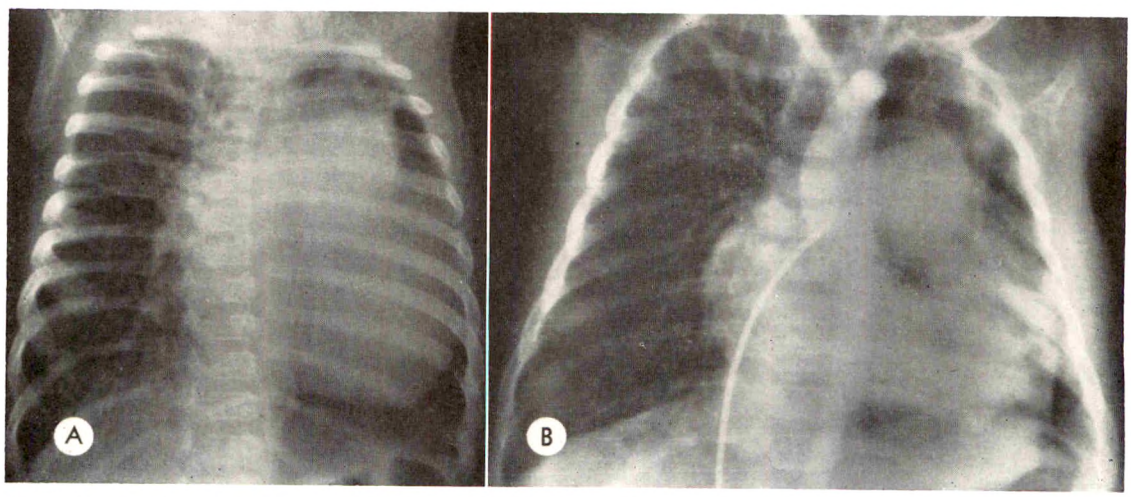


FIG. 2. Case II. (*A*) Frontal roentgenogram of the chest. The heart is enlarged. The lungs are overaerated and the vascular markings in the left lung are absent. The main and left pulmonary arteries are dilated. (*B*) Venous angiogram and retrograde aortogram. The pulmonary artery and its main branches are dilated.

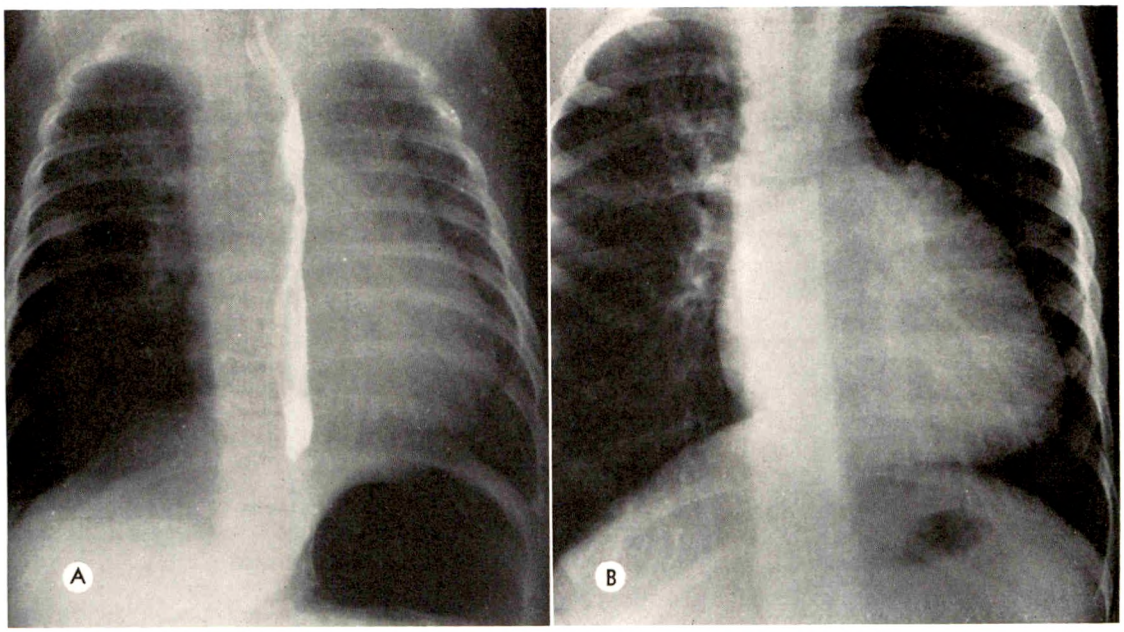


Fig. 3. Case III. (*A*) Frontal roentgenogram of the chest at 2 months of age. The heart is moderately enlarged. The pulmonary arteries are not conspicuously dilated. The right lung is overaerated. (*B*) Frontal roentgenogram of the chest at 6 years of age. The heart is enlarged. The main and right pulmonary arteries are slightly dilated.

cal examination disclosed respiratory wheezes and scattered coarse rales. A Grade 4 to-and-fro murmur heard over the entire precordium radiated to the axilla. P2 was not audible. The liver edge was palpated 6 cm. below the right costal margin.

There was right ventricular hypertrophy on electrocardiography.

Roentgenogram of the chest (Fig. 3*A*) showed moderate cardiomegaly. The pulmonary arteries were not conspicuously dilated. The right lung was emphysematous. On bronchography the right main stem bronchus was narrow during inspiration; its lumen was completely obliterated during expiration.

Cineangiocardiography demonstrated that the main and right pulmonary arteries were dilated and that there were ventricular septal defect, pulmonary stenosis, and right-sided aortic arch present.

At surgery the dilated right pulmonary artery compressed the right main stem bronchus. The cusps of the pulmonary valve were absent. Aneurysmorrhaphy of the right pulmonary artery was performed. Biopsy of the wall of the dilated pulmonary artery showed normal histologic findings.

Although the infant's clinical condition improved after surgery, he has remained dyspneic. At 6 years of age his chest roentgenogram (Fig. 3*B*) again showed cardiomegaly with slight dilatation of the pulmonary artery and its right main branch.

Case IV. J.S., a 3 month old white girl, was admitted to Children's Hospital of Pittsburgh on December 4, 1964 because of cough and wheezing beginning at 2 weeks of age. She was slightly cyanotic at birth and had been placed in oxygen for 24 hours. On physical examination she was in moderate respiratory distress but was not cyanotic on crying. She wheezed moderately during expiration. A Grade 3–4 systolic murmur and a Grade 1 diastolic murmur heard over the entire precordium were maximal at the lower left sternal border. The second pulmonary sound was diminished.

Electrocardiography showed right ventricular hypertrophy.

Roentgenogram of the chest disclosed cardiomegaly and overaeration of the right lung. The pulmonary arteries were markedly dilated. Bronchograms showed that the tracheal lumen was obliterated on expiration. Cineangiocardiography confirmed the dilatation of the pulmonary artery and its main branches and demon-

strated ventricular septal defect, pulmonary stenosis, and right-sided aortic arch.

The infant died before surgery could be accomplished to relieve the compression of the trachea by the dilated pulmonary artery.

At necropsy aneurysmal dilatation of the main pulmonary artery and both its branches compressed the lower part of the trachea. There was a large ventricular septal defect; the aorta was right-sided. The pulmonary valve cusps were absent, the pulmonary valvular ring was narrow, and the infundibulum of the pulmonary artery was stenotic. Pulmonary venous drainage and the coronary sinus were normal. The wall of the right ventricle was hypertrophied. The ductus arteriosus was not patent. The wall of the dilated pulmonary artery was not examined microscopically.

CASE V. C.L., a white girl 2 months of age, was admitted to Children's Hospital of Pittsburgh on September 10, 1962 because of intermittent spells of cyanosis and heart murmur since birth. She had coughed, wheezed, and been febrile for 2 weeks. On physical examination a harsh, blowing Grade 4–6 to-and-fro murmur was heard over the entire precordium; it was loudest in the third and fourth intercostal spaces. The second pulmonary sound was not audible. There were bilateral expiratory wheezes.

Electrocardiography showed right axis deviation and right ventricular hypertrophy.

On chest roentgenography the heart was enlarged, the pulmonary arteries were prominent, and the vascularity in the lungs was increased. Cineangiocardiography revealed moderately dilated pulmonary arteries, ventricular septal defect, and pulmonary stenosis.

At 8 months of age the patient was explored surgically and a ventricular septal defect was closed. The pulmonary valve cusps were rudimentary and the pulmonary infundibulum was stenosed. The child has developed normally since surgery but has slight dyspnea on exertion.

CASE VI. K.Mc., a white boy 8 months of age, was admitted to Children's Hospital of Pittsburgh on January 4, 1960 because of rapid respiration and recurrent episodes of wheezing, which began at 3 months of age. On the third day of life he had had a cyanotic episode and a heart murmur was detected. Physical examination showed a slightly cyanotic infant in moderate respiratory distress. Auscultation revealed bilateral expiratory wheezes. A Grade 4–6 to-and-fro murmur was heard over the precordium, loudest along the lower left sternal border. P2 was not audible.

Electrocardiography showed right axis deviation with right atrial and right ventricular hypertrophy.

Roentgenogram of the chest (Fig. 4*A*) showed moderate cardiomegaly and normally prominent pulmonary artery and its main branches. The aorta was right-sided. The right middle and lower lobes were emphysematous. Bronchogram (Fig. 4*B*) revealed extrinsic pressure on the right middle and lower lobe bronchi. Cineangiocardiography (Fig. 4, *C* and *D*) showed a moderately dilated pulmonary artery and its right main branch, ventricular septal defect, and pulmonary stenosis. The left pulmonary artery was slightly dilated.

Aneurysmorrhaphy of the right pulmonary artery was done to relieve the pressure on the right main stem bronchus. The cusps of the pulmonary valve were absent. The child progressed satisfactorily after surgery but slight exertional dyspnea continued. At 8 years his height and weight measurements were at the tenth percentile for the age.

Chest roentgenograms showed persistent cardiomegaly with prominent pulmonary arteries.

CASE VII. E.M., a white girl 7 days of age, was admitted to Children's Hospital of Pittsburgh on February 14, 1958 for evaluation of heart murmur discovered immediately after birth and because she became cyanotic on crying. On physical examination she was neither cyanotic nor dyspneic. Her lungs were clear. There was a Grade 3 to-and-fro murmur over the entire chest loudest over the lower left sternal border. P2 was absent.

Electrocardiography showed abnormal right ventricular hypertrophy.

Chest roentgenogram (Fig. 5*A*) and fluoroscopy showed moderate cardiomegaly with a left-sided rounded pulsating hilar mass of water density that displaced the barium filled esophagus posteriorly and to the right. The left lung was overaerated. Angiocardiography (Fig. 5*B*) showed aneurysmal dilatation of the main and left pulmonary arteries, ventricular septal defect, and right-sided aorta.

At surgery the pulsating mass was identified

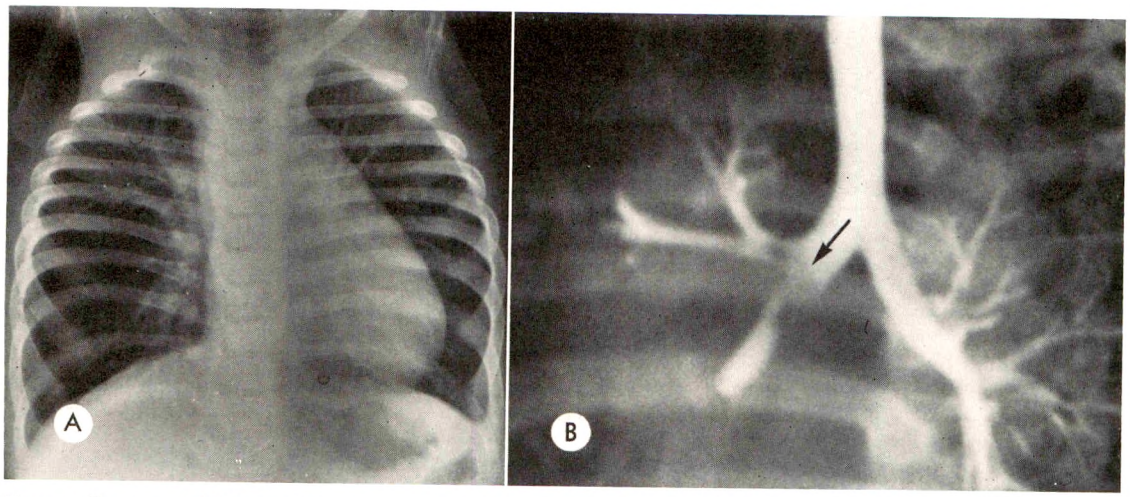


FIG. 4. Case VI. (*A*) Frontal roentgenogram of the chest. The heart is slightly enlarged. The pulmonary arteries are normally prominent. The right middle and lower lobes are overaerated. (*B*) Tracheobronchogram. The right middle and lower lobe bronchi are compressed (arrow).

as dilated left pulmonary artery. Aneurysmorrhaphy of the left pulmonary artery was done to relieve pressure on the left main stem bronchus. The infant suffered respiratory arrest and died after surgery.

At necropsy the pulmonary artery and its left main branch were markedly dilated. The right pulmonary artery was moderately dilated. The pulmonary valve consisted of a fibrous ring without valve leaflets. The dilatation of the pulmonary artery involved the valvular area, and the adjacent myocardial wall was thin. The right ventricle was hypertrophied and dilated. A large high ventricular septal defect was present. The aorta was right-sided.

Microscopically the intrapulmonary arteries and interalveolar capillaries were markedly dilated and some peripheral pulmonary artery branches showed irregular intimal thickening. The wall of the main pulmonary artery was not examined histologically.

CASE VIII. D.M., a $2\frac{1}{2}$ year old Negro boy, was admitted to Children's Hospital of Pittsburgh on August 5, 1959 because of heart murmur and failure to thrive. He was not cyanotic.

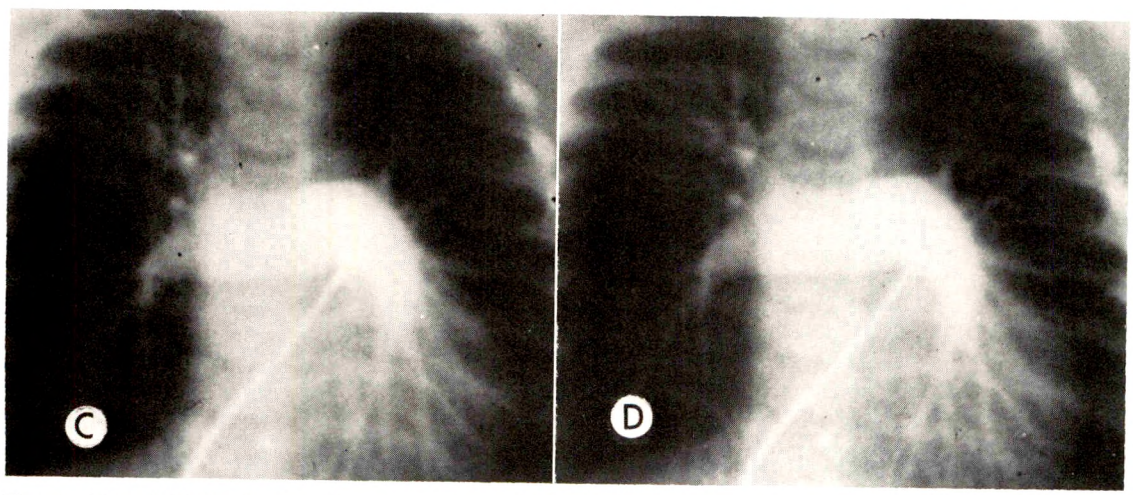


FIG. 4. (*C* and *D*) In the cine films the main and right pulmonary arteries are moderately dilated; the left pulmonary artery is slightly dilated.

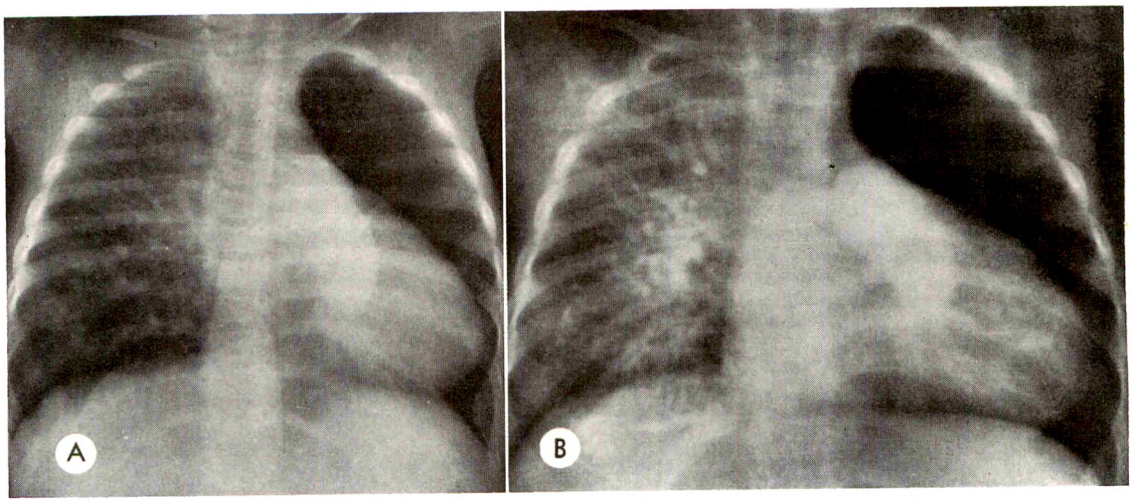


FIG. 5. Case VII. (*A*) Frontal roentgenogram of the chest. The heart is enlarged. The left pulmonary artery is dilated. The left lung is overaerated. (*B*) Angiocardiogram. The main and left pulmonary arteries are dilated. The left lung is overaerated.

His lungs were clear. A thrill was palpated at the lower left sternal border. A Grade 3 to-and-fro murmur was heard in the third and fourth intercostal spaces along the left sternal border. P2 was clearly heard and equal to A2.

Electrocardiography showed right axis deviation and right ventricular hypertrophy.

Chest roentgenogram (Fig. 6*A*) demonstrated moderate cardiomegaly with normally prominent pulmonary arteries. Cardioangiography showed slight prominence of the pulmonary arteries and no other cardiac malformation.

Because pulmonary stenosis was thought to be present at cardiac catheterization, the child was explored surgically. His main pulmonary artery was described as "tense." During operation the pressure in both the pulmonary artery and in the right ventricle was 80/0 mm. Hg.The pulmonary valve cusps were absent and there was no evidence of pulmonary stenosis.

The child's condition did not change after

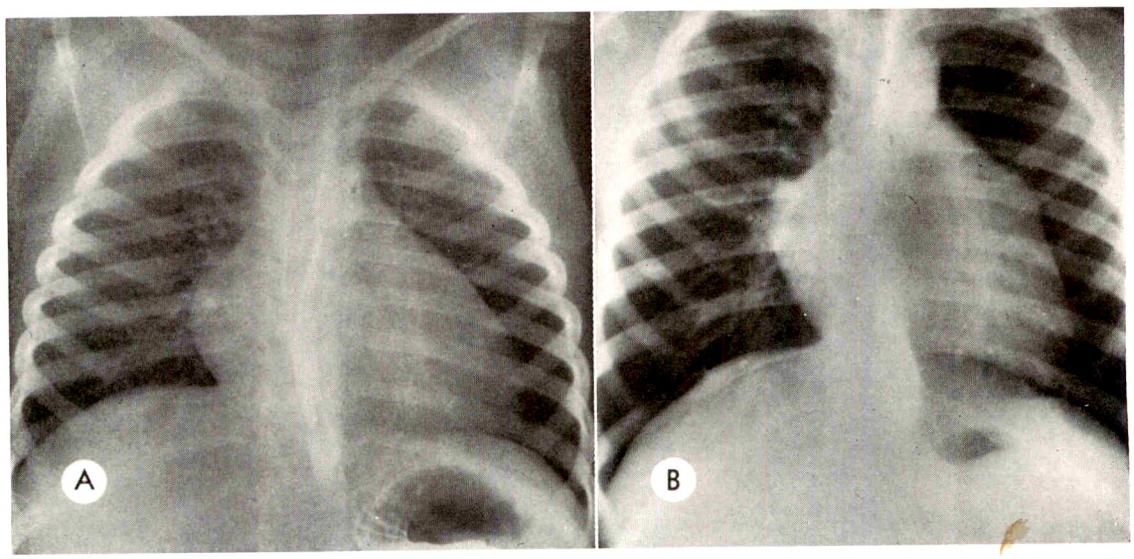


FIG. 6. Case VIII. (*A*) Frontal roentgenogram of the chest at 2½ years of age. The heart is enlarged. The pulmonary arteries are normal. (*B*) Frontal roentgenogram of the chest at 11 years of age. The heart is enlarged and the pulmonary arteries are prominent.

surgery. At 11 years of age his height and weight measurements were at the third percentile for his age; repeated cardiac catheterizations showed no pressure gradient between the right ventricle and the main pulmonary artery.

Roentgenogram of the chest (Fig. 6*B*) again showed cardiomegaly and slight prominence of the pulmonary arteries.

CARDIAC CATHETERIZATION (Table I)

Six children were catheterized; 5 showed ventricular septal defects and pulmonary stenosis. The sixth had isolated absence of the pulmonary valve cusps. The catheter was able to be passed into the main pulmonary artery in 4 patients with ventricular septal defects in whom pressure gradients between the pulmonary artery and right ventricle indicated pulmonary stenosis. All 6 patients showed normal right ventricular end diastolic pressures and normal mean right atrial pressures. Three children showed both left-to-right and right-to-left shunts; 1 child showed left-to-right shunt only. In the child (Case VIII) with isolated absence of the pulmonary valve, cardiac catheterization at 3 years of age showed high right ventricular pressure reaching systemic level with pressure gradient between main pulmonary artery and right ventricle indicating pulmonary stenosis. At operation 1 week later, direct measurement of pressure showed that the pressure was not as elevated and there was no evidence of pulmonary stenosis. Cardiac catheterization when the child was 11 years of age showed no pressure gradient and the right ventricular pressure was lower than at the earlier catheterization.

CINEANGIOCARDIOGRAPHIC FINDINGS (Table II)

Seven patients had angiocardiograms. The pulmonary artery and its right main branch were markedly dilated in 4 children and moderately dilated in 3. The left pulmonary artery was markedly dilated in 1 patient, moderately dilated in 5, and was normal in 1 child. Six patients had ventricular septal defects and pulmonary stenosis, 3 had right-sided aortic arch and 2 had patent foramen ovale. One child had isolated absence of the pulmonary valve cusps.

In 2 children (Cases III and VI) cineangiocardiography showed dilatation of the pulmonary arteries which was not evident on the chest roentgenograms.

REVIEW OF THE LITERATURE

The available literature includes 40 cases of absence of the pulmonary valve cusps. Chevers[4] in 1847 first described this cardiac malformation associated with ventricular septal defect and patent foramen ovale at necropsy of an 8 year old child who had had a to-and-fro murmur at the lower left sternal border and was slightly cyanotic. Kurtz *et al.*[12] in 1927 described an 11 year old boy who had been dyspneic, slightly cyanotic, and had a to-and-fro murmur at the lower left sternal border and who at necropsy was found to have pulmonary stenosis, ventricular septal defect and absent pulmonary valve cusps. In 1954, Lavennes and associ-

TABLE I

CARDIAC CATHETERIZATION FINDINGS

Patient	Age at Catheterization	Pressure (mm. Hg)					O_2 Saturation (per cent)						Shunt	
		*RA Mean	RV	PA	A°	BA°	SVC	RA	RV	PA	A°	BA°	L to R	R to L
J.S. (Case IV)	3 mo.		69/3	26/4										
E.O. (Case III)	3 mo.	1	66/2	14/4	66/35		60	62	68	74	78		+	+
M.S. (Case I)	4 da.	1	81/5			88/49	63	64	68			82	+	+
C.L. (Case V)	2 yr.	1	78/4	27/7	100/58		71	72	80	77	94		+	+
K.Mc. (Case VI)	8 yr.	1	95/5	26/4		110/51	73	75	80	80	96		+	−
D.M. (Case VIII)	3 yr.		108/5	22/12	106/51/		7.96	8.41	7.55	7.36	12.1 vol. %		−	−
D.M. At operation	3 yr.		80/0	80/0										
D.M. Repeat catheterization	11 yr.	2	67/6	67/8	115/71	111/66	79	79	80	80		96	−	−

* RA—right auricle; RV—right ventricle; PA—pulmonary artery; A°—aorta; BA°—brachial artery; SVC—superior vena cava.

TABLE II

CINEANGIOCARDIOGRAPHIC FINDINGS

Patient	Aneurysmal Dilatation of Pulmonary Artery			Tracheal Compression	Diagnosis
	Main	Right	Left		
J.S. (Case IV)	++	++	++	+	*VSD, PS, Rt. A.° Arch
T.M. (Case II)	+	+	+	+	VSD, PS, PFO
E.O. (Case III)	++	++	−	+	VSD, PS, Rt. A.° Arch
M.S. (Case I)	++	++	+	+	VSD, PS, PFO
C.L. (Case V)	+	+	+	−	VSD, PS
K.Mc. (Case VI)	++	++	+	+	VSD, PS, Rt. A.° Arch
D.M. (Case VIII)	+	+	+	−	

* VSD—patency of the interventricular septum; PS—pulmonary stenosis; Rt.—right; A.° Arch—aortic arch; PFO—patent foramen ovale.

ates[13] reported the clinical and necropsy findings in a 46 year old woman who had the Eisenmenger complex and pulmonary insufficiency presumably due to absence of the pulmonary valve cusps. Ehrenhaft[7] in 1955 described the first case of solitary absence of the pulmonary valve cusps discovered at surgery in a boy 14 years of age. The child had dyspnea and decreased exercise tolerance since the age of 4. Ehrenhaft thought that rheumatic fever or bacterial endocarditis had destroyed the valve cusps. Campeau *et al.*[2] in 1957 reported a 32 year old male in whom the malformation was identified at necropsy; there were a large ventricular septal defect and a single coronary artery. The patient had a long history of exertional dyspnea with cyanosis; at 18 years of age he developed heart failure. In 1958 Onesti and Harned[16] described a slightly cyanotic, wheezing 5 week old white boy who at necropsy had absent pulmonary valve cusps and ventricular and atrial septal defects. In 1959 Smith *et al.*[21] reported the necropsy findings in 2 children who were cyanotic and had to-and-fro murmurs along the left sternal border: a $4\frac{1}{2}$ year old boy who had tetralogy of Fallot as well as absent pulmonary valve cusps, and a 1 day old prematurely born infant who had isolated absence of the pulmonary valve cusps, fetal hydrops and meningoencephalocele. The necropsy findings in the premature infant were presented as evidence of the probable congenital origin of the pulmonary valve cusps. Vlad *et al.*[23] in 1960 reported the clinical and postmortem findings in 6 children whose ages ranged from 2 days to 14 years. In 5, the second pulmonary sound had been absent or markedly diminished. At necropsy the right ventricle was more hypertrophied than expected from the dominant heart lesion. Anselmi *et al.*[1] in 1960 found absence of pulmonary valve cusps at necropsy in 2 patients. Because the first child wheezed and had had a continuous murmur, a clinical diagnosis of patency of the ductus arteriosus associated with a vascular ring had been made. In a second child, cyanosis and a double murmur in the pulmonary area had led to an incorrect diagnosis of persistent truncus arteriosus. In 1961 Gasul and his colleagues[10] found absence of pulmonary valve cusps at necropsy in a $7\frac{1}{2}$ year old boy who had been slightly cyanotic and had been considered to have tetralogy of Fallot. Campeau *et al.*[3] in the same year described the clinical and autopsy findings in 2 patients with absent pulmonary valve cusps. Their first patient had ventricular septal defect and infundibular pulmonary stenosis; the second had aortic sinus of Valsalva. In these 2 patients, absence of the pulmonary valve cusps had been associated with clinical signs of insufficiency of the pulmonary valve. Campeau *et al.*[3] suggested

that the combination of absent pulmonary valve cusps and abnormally large aortic cusps resulted from unequal embryologic division of the truncus arteriosus. In 1961 Sinton[20] reported the findings of absence of pulmonary valve cusps and large ventricular septal defect at necropsy in a child 3 months of age. Ito *et al.*[11] in 1961 reported isolated absence of the pulmonary valve in a 2 day old white boy who became deeply cyanotic 24 hours after birth and died in congestive heart failure with generalized edema of the face and extremities. In 1962, Venables[22] described 2 infants with intractable heart failure who at necropsy had ventricular septal defect and absent pulmonary valve cusps. Miller and his associates [14,15] in 1958 and 1962 described 7 patients with tetralogy of Fallot and absent pulmonary valve cusps. Miller suggested that tetralogy of Fallot with free pulmonary regurgitation and aneurysm of the pulmonary artery constituted a distinct clinical syndrome which should permit clinical diagnosis of associated absence of the pulmonary valve. Elliott *et al.*[8] in 1962 found ventricular septal defect and absent pulmonary valve cusps at necropsy in a 5 week old boy and directed attention to the fact that 15 out of 16 reported cases with absent pulmonary valve cusps were males. D'Cruze *et al.*[6] in 1964 summarized the clinical and pathologic findings in 5 infants in whom this anomaly was demonstrated at necropsy. Three patients had associated tetralogy of Fallot. In a fourth infant overriding aorta and pulmonary stenosis were not conspicuous. The fifth infant had double-outlet right ventricle. large atrioventricular canal, an abnormal communication of the posterior aortic sinus of Valsalva with the right ventricle, and a single coronary artery. D'Cruz *et al.*[6] stressed the importance of respiratory obstruction caused by the marked dilatation of the pulmonary arteries. Childers and McCrea[5] in 1964 reported the clinical and necropsy findings of a 30 year old woman with Marfan's syndrome, ventricular septal defect, aneurysm of an aortic sinus of Valsalva and absence of the pulmonary valve cusps. The patient had congenital heart disease and repeated pulmonary infections from infancy. There were medial mucoid degeneration and small cyst formation with focal disintegration and interruption of elastic lamina in the wall of the dilated pulmonary artery. Ruttenberg *et al.*[18] in 1964 reported 2 cases and emphasized the usefulness of angiocardiographic examinations in defining the anatomic and hemodynamic characteristics of this anomaly associated with tetralogy of Fallot. Pouget *et al.*[17] in 1967 reported a 73 year old man with myelomatosis in whom isolated absence of the pulmonary valve cusps was discovered as an incidental finding at necropsy.

DISCUSSION

The clinical and roentgenographic features that accompany absence of the pulmonary valve cusps associated with other congenital cardiac malformations are characteristic. They include respiratory distress with wheezing, to-and-fro murmurs along the lower left sternal border, absent or diminished second pulmonary sounds, enlarged pulmonary arteries and right ventricular hypertrophy. Seven of our patients had respiratory distress, wheezing, slight cyanosis and absent or diminished second pulmonary sounds. All 8 children had to-and-fro murmurs. Wheezing, slight cyanosis and to-and-fro murmurs were present in the large majority of patients reported in the literature. The only patient with isolated absence of the pulmonary valve cusps discussed in this report did not have respiratory distress. His second pulmonary sound was clearly audible and was equal to the second aortic sound.

Chest roentgenograms showed obstructive emphysema of the right lung in 5 children and of the left lung in 1 child; the lungs of 2 children were normally aerated. The pulmonary artery and its right main branch were markedly dilated in 4, moderately dilated in 3, and slightly dilated in 1 of our patients. The left pulmonary artery

was markedly dilated in 1 patient, moderately dilated in 6 and was not dilated in 1 patient. In the child with isolated absence of the pulmonary valve cusps, the pulmonary arteries were not as conspicuously dilated as in the patients with associated cardiac malformations. This probably explains his lack of respiratory distress.

The cause of the aneurysmal dilatation of the pulmonary arteries is not certain; it may result from increased right ventricular and stroke volumes due to pulmonary incompetence and left-to-right shunt through ventricular septal defects. Childers and McCrea[5] thought that inherent intrinsic disease of the pulmonary artery wall was a possible cause. They found mucoid degeneration with focal disintegration and interruption of elastic lamina in the dilated pulmonary artery of their patient with absent pulmonary valve cusps. Saldaña and Arias-Stella,[19] however, noted similar fragmentation and interruption of elastic fibers in the walls of the pulmonary artery of normal infants and children between 25 days and 3 years of age. In 3 patients reported in this paper the walls of the pulmonary arteries were histologically normal.

Bronchograms were obtained in 5 children. In each a dilated pulmonary artery compressed the lumen of the trachea or main stem bronchus. D'Cruz *et al.*[6] in 1964 was the first to stress the importance of respiratory obstruction associated with congenital absence of the pulmonary valve cusps. In 1960 Anselmi *et al.*[1] found no pulmonary valve cusps at necropsy in a child who had wheezed, had had a continuous murmur, had roentgenologic evidence of extrinsic pressure on the trachea and had been mistakenly diagnosed clinically as patency of the ductus arteriosus and vascular ring. Angiocardiography demonstrates the dilatation of pulmonary arteries which may not be evident on chest roentgenograms and identifies associated cardiac anomalies. It does not reliably demonstrate the absence of pulmonary valve cusps.

D'Cruz *et al.*[6] noted that congenital absence of the pulmonary valve cusps was more common in males. Of 36 reported cases in which sex was stated, 24 were males. In our group of 8 patients, five were girls.

Tetralogy of Fallot is the most common cardiac malformation associated with absence of the pulmonary valve leaflets. Other associated anomalies include ventricular septal defects, atrial septal defects, aneurysm of an aortic sinus of Valsalva, single coronary artery, atrioventricular canal, tricuspid and mitral atresia, patent ductus arteriosus, and Marfan's syndrome.

Patients with isolated absence of the pulmonary valve cusps have not had respiratory distress and seem to tolerate the lesion well. Our patient with isolated absence of the pulmonary valve cusps is the fifth reported in the literature. He was admitted to the hospital at $2\frac{1}{2}$ years of age because of heart murmur and failure to thrive. He is living and doing well at 11 years of age. Pouget and his associates[17] in 1967 found isolated absence of the pulmonary valve cusps as an incidental finding at necropsy in a 73 year old man who died with cerebral infarction. Ehrenhaft[7] reported isolated absence of pulmonary valve cusps in a 14 year old boy who was dyspneic and had decreased exercise tolerance. Ellison *et al.*[9] demonstrated that dogs continue their normal activities following pulmonary valvectomy.

SUMMARY AND CONCLUSIONS

1. The clinical and roentgenologic findings in 8 infants with absent pulmonary valve leaflets are discussed.

2. Repeated respiratory distress with wheezing, to-and-fro murmurs along the lower left sternal border, absent or diminished second pulmonary sounds, enlarged pulmonary arteries and right ventricular hypertrophy are characteristic of absent pulmonary valve cusps associated with other congenital cardiac malformations.

3. The only patient with isolated absence

of the pulmonary valve cusps discussed in this report did not have respiratory distress and his pulmonary arteries were not as conspicuously dilated as in patients with associated cardiac malformations.

4. The literature on absence of pulmonary valve leaflets is reviewed.

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ANGIOGRAPHIC DEMONSTRATION OF SYSTEMIC ARTERIAL SUPPLY IN ABNORMAL PULMONARY CIRCULATION*

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A SYSTEMIC arterial supply is uncommon in patients with anomalies of the pulmonary circulation. Anomalous pulmonary venous drainage of the right lung into the inferior vena cava, absent unilateral pulmonary artery, and sequestration of the lung have been reported to be associated with an anomalous systemic arterial supply from the thoracic or abdominal aorta and its main branches. The systemic arterial collateral circulation in congenital heart disease with decreased pulmonary blood flow is well known. Most publications on these anomalies are, however, based on operative or postmortem findings, only few being concerned with the angiographic appearance of the anomalous arteries. To our knowledge the literature contains no reports of selective angiography of the aortic branches in cases of anomalous drainage of the right lung or absent unilateral pulmonary artery.

This paper illustrates the value of selective angiography in the preoperative investigation of an abnormal pulmonary circulation.

MATERIAL AND RESULTS

HYPOPLASIA OR ABSENCE OF THE RIGHT PULMONARY ARTERY WITH OR WITHOUT ANOMALOUS PULMONARY VENOUS DRAINAGE

Four patients with anomalous pulmonary venous drainage of the right lung were examined with angiocardiography or pulmonary angiography. In 1 of the cases the examination also included selective celiac arteriography and bronchography. At routine chest examination the right hemithorax was smaller than the left with displacement of the mediastinal structures to the right (Fig. 1, *A* and *B*). In 3 patients the anomalous pulmonary right vein ran parallel to the right border of the heart. In the fourth patient the vein was masked by the increased density of the right hemithorax.

At pulmonary angiography the right pulmonary artery proved hypoplastic in 3 of

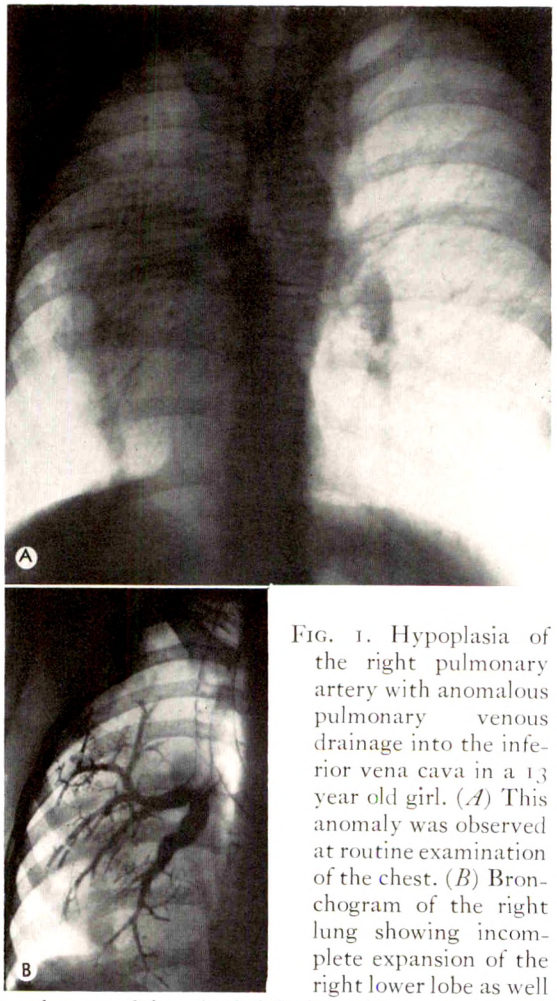


FIG. 1. Hypoplasia of the right pulmonary artery with anomalous pulmonary venous drainage into the inferior vena cava in a 13 year old girl. (*A*) This anomaly was observed at routine examination of the chest. (*B*) Bronchogram of the right lung showing incomplete expansion of the right lower lobe as well as absence of the middle lobe bronchus.

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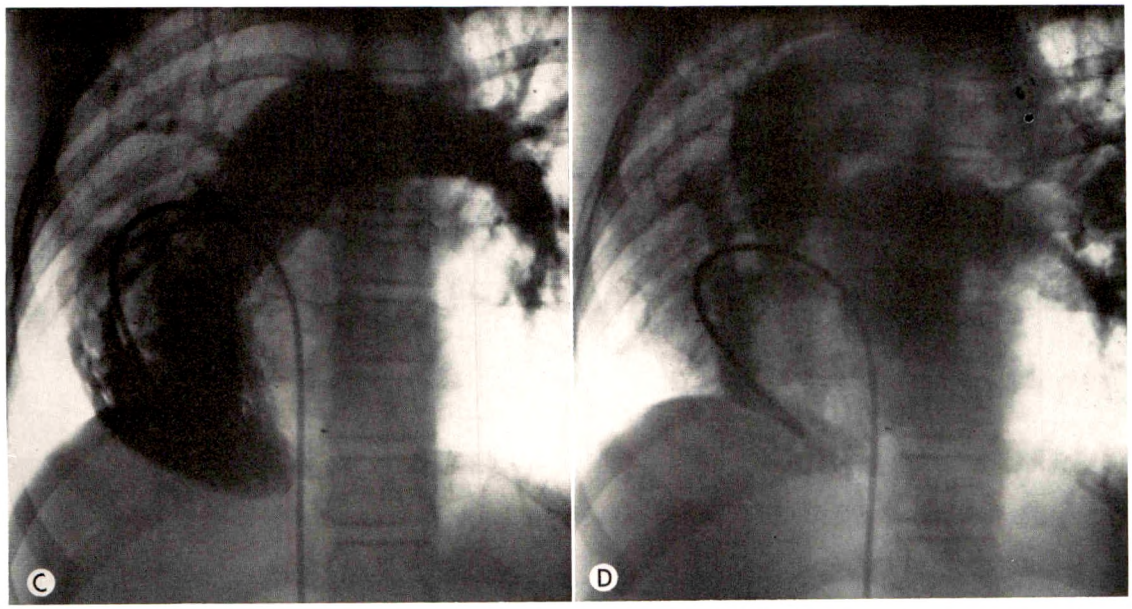


Fig. 1. (*C* and *D*) Angiograms show dextroposition of the right ventricle and anomalous pulmonary circulation of the right lung.

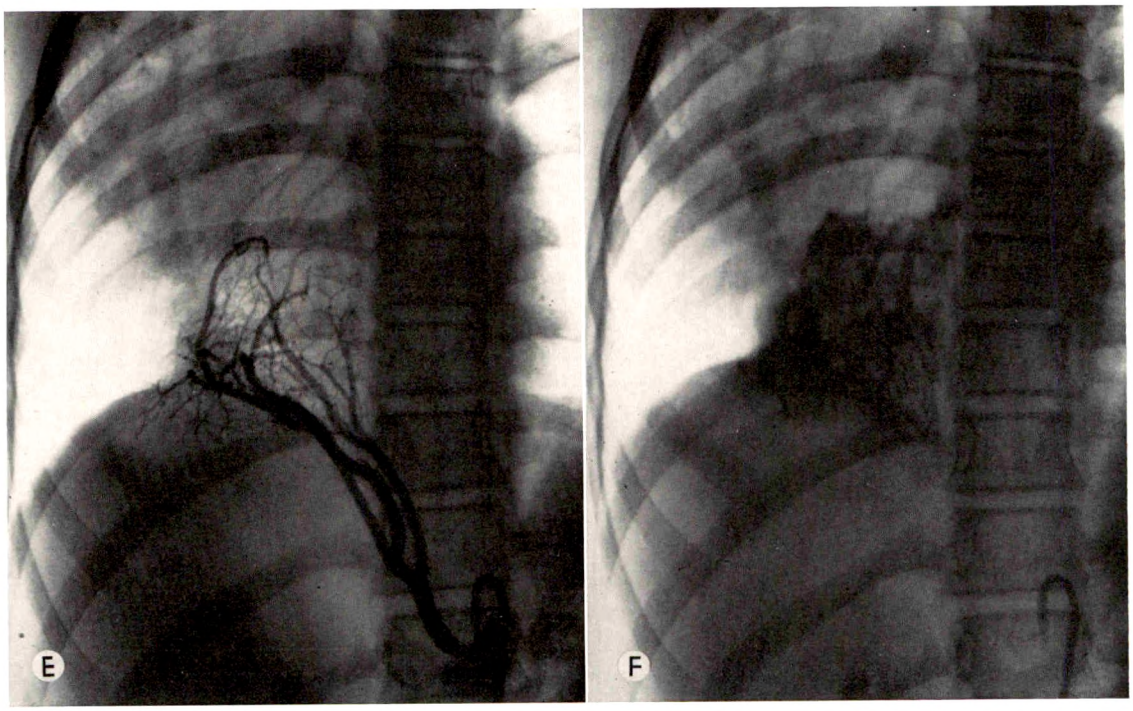


Fig. 1. (*E* and *F*) Celiac angiograms demonstrate an anomalous systemic artery arising from the celiac axis and supplying the small lower lobe of the right lung. The veins of this lobe enter the left atrium.

the cases and the appearance of its branches and their distribution in the right lung was abnormal (Fig. 1*C*). Those parts of the right lung supplied by the hypoplastic pulmonary artery were drained into the inferior vena cava in 2 patients (Fig. 1*D*), while in 1 the upper part of the lung was drained into the left atrium. In all 3 patients with a hypoplastic right lung, branches of the abdominal aorta supplied the right lower lobe. One of these patients was examined with selective celiac angiography, at which an anomalous artery arising from the celiac axis was demonstrated. The artery ran craniad and branched in the small lower lobe of the right lung, which had no blood supply from the lesser circulation (Fig. 1*E*). The vein draining this lobe emptied into the left atrium (Fig. 1*F*). In this case, the absence of the middle lobe bronchus was disclosed at bronchography (Fig. 1*B*). The patient presented in Figure 1 was operated upon and the angiographic findings were verified. A large vein of the lower lobe entered the left atrium and several small veins of this lobe joined the anomalous pulmonary vein running from the large upper lobe to the inferior vena cava. In the other 2 patients the aberrant systemic vessels came from the level previously demonstrated but it could not be decided whether they arose from the aorta or the celiac axis. The arteries supplied the right lower lobe. Their venous drainage, however, could not be demonstrated because of the low density of the contrast medium. In 1 of these 2 cases, operation and postmortem examination confirmed that at least 2 veins arose from the right lung and entered the inferior vena cava just proximal to the hepatic vein below the diaphragm. No pulmonary vein emptied into the left atrium. The systemic arteries arising from the abdominal aorta proximal to the origin of the celiac axis supplied the right lower lobe.

In the fourth patient with anomalous pulmonary venous drainage, no right pulmonary artery was demonstrated at angiocardiography. But the right lung was supplied by wide arteries arising from the abdominal aorta at the level of the celiac axis. The pulmonary veins entered the inferior vena cava. Right pneumonectomy was performed and the angiographic findings were verified.

One additional patient had no right pulmonary artery, but the venous drainage of the anomalous lung was normal. The right hemithorax was small and the mediastinum was displaced to the right (Fig. 2*A*). The bronchogram demonstrated that the intermediary trunk of the right bronchus ended blindly and that the distribution of the upper lobe bronchus was anomalous (Fig. 2*B*). At pulmonary angiography the right pulmonary artery was found to be absent (Fig. 2*C*). At selective celiac angiography the entire hypoplastic lung proved to be supplied by an anomalous systemic artery arising from the celiac axis (Fig. 2*D*). The right lung was drained into the left atrium (Fig. 2*E*). The patient had no symptoms. No operation was performed.

INTRALOBAR SEQUESTRATION OF THE LOWER LOBE OF THE LEFT LUNG

Two patients were examined with bronchography as well as selective angiography. At angiography an aberrant artery was demonstrated in each of them; it arose from the distal part of the thoracic aorta and branched into the mass demonstrated in the plain roentgenogram of the chest (Fig. 3*A*). In the capillary phase cystic areas were seen (Fig. 3*B*). The vein of the lesion entered the left atrium (Fig. 3*C*). Bronchographic examination revealed nothing remarkable except slight displacement with poor filling of the bronchus of the left posterobasal segment around the lesion. Operation confirmed the angiographic findings.

PULMONARY ATRESIA WITH LARGE VENTRICULAR SEPTAL DEFECT

Two patients with pulmonary atresia were submitted to angiography. In both cases the outflow tract of the right ventricle ended blindly without infundibular stenosis but with a large ventricular septal defect (Fig. 4, *A* and *B*). In both cases, at selec-

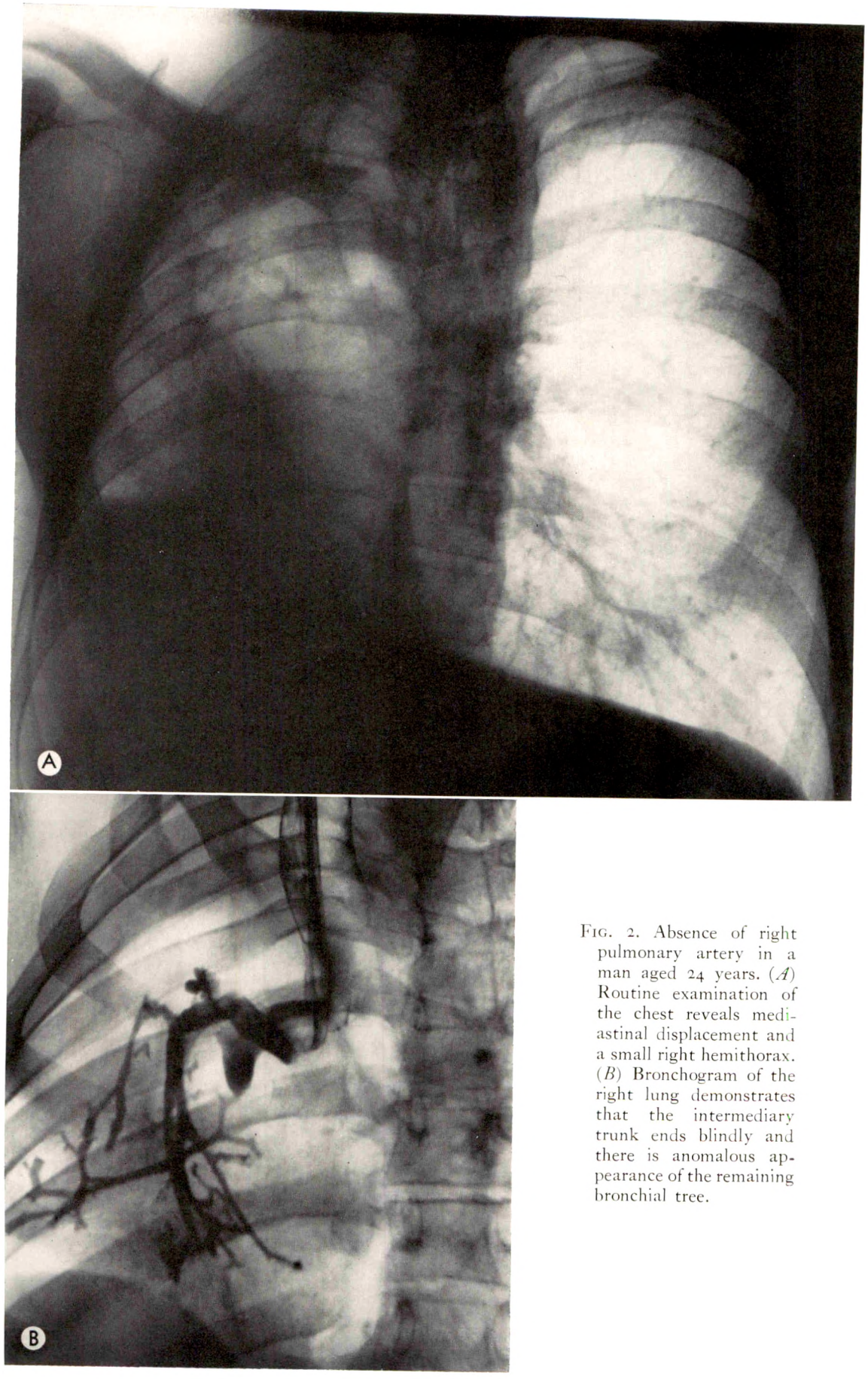


FIG. 2. Absence of right pulmonary artery in a man aged 24 years. (*A*) Routine examination of the chest reveals mediastinal displacement and a small right hemithorax. (*B*) Bronchogram of the right lung demonstrates that the intermediary trunk ends blindly and there is anomalous appearance of the remaining bronchial tree.



FIG. 2. (*C*) Pulmonary angiogram shows dextroposition as well as absence of the right pulmonary artery.

tive angiography and thoracic aortography, the pulmonary arteries were found to be connected with the descending aorta. Multiple branches ran to both lungs (Fig. 4, *C-E*; and 5, *A* and *B*). The connection between the pulmonary arteries and the aorta did not appear to consist of bronchial arteries. In 1 patient a branch of the pulmonary artery of the left upper lobe was connected with a pulmonary artery of the

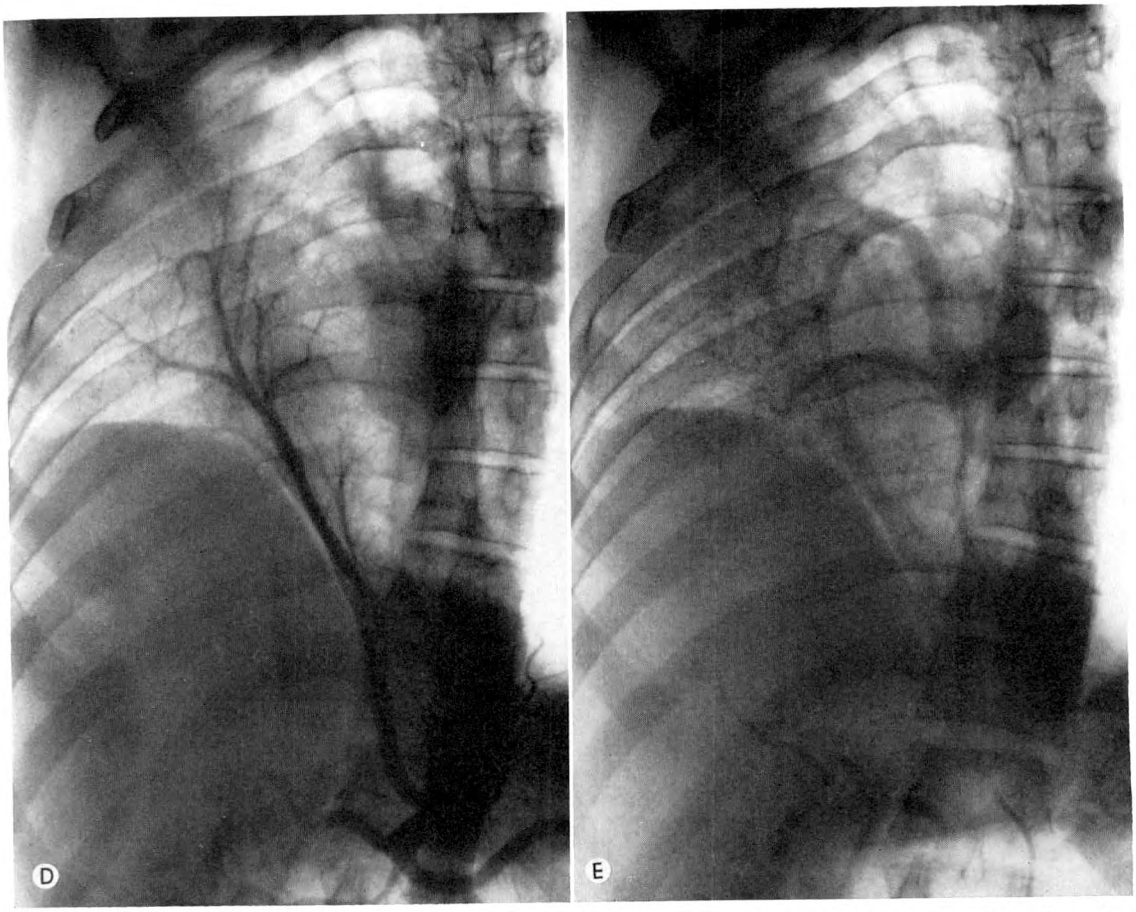


FIG. 2. (*D* and *E*) Selective celiac angiograms show that an anomalous systemic artery arises from the celiac axis and supplies the entire right lung. The veins enter the left atrium.

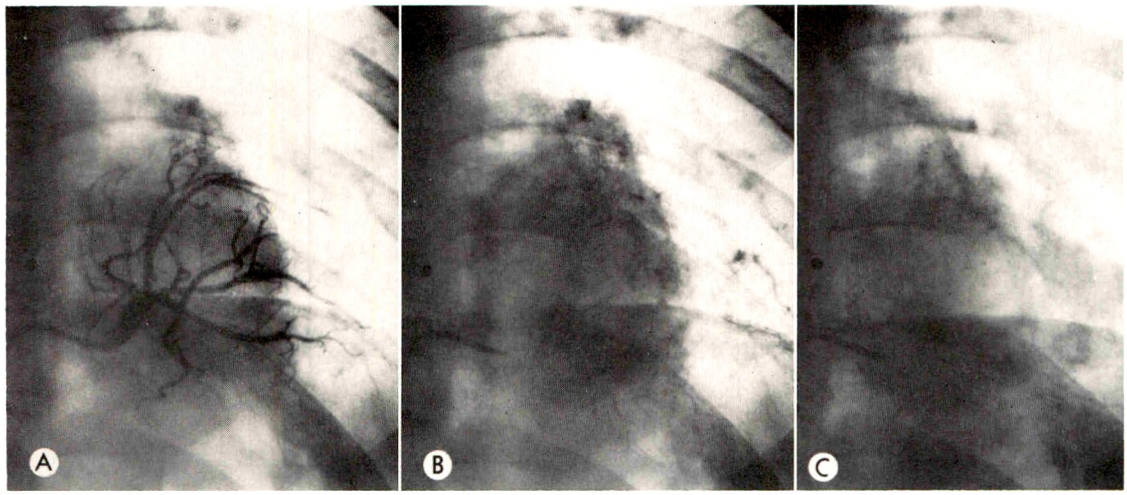


Fig. 3. Intralobar sequestration of the left lung in a man aged 20 years. (*A*) Selective angiography shows an aberrant artery arising from the distal part of the thoracic aorta and supplying a mass in the left lower lobe. (*B*) The tumor has a cystic appearance. (*C*) The veins enter the left atrium.

right middle lobe (Fig. 4, *D* and *E*) and two further arteries supplied the left lung and at least one, the right (Fig. 4*C*). In the second patient two pulmonary arteries communicated with the descending aorta and ran to the left lung and at least one artery to the right lung. Thanks to the selective injection of the contrast medium, the pulmonary veins were shown to empty into the left atrium (Fig. 4*F*). At bronchial angiography of 1 of the patients bronchopulmonary connections with a distal filling of the pulmonary arteries were found (Fig. 5*C*).

DISCUSSION

According to a review by Ferencz,[6] an aberrant systemic arterial supply may be associated with a wide variety of anomalies of the lung and the pulmonary circulation. The severity depends on the stage of embryologic development at which the normal process of development is disturbed.[8] Anomalous drainage of the pulmonary vein is regarded as the result of a persistent connection between the pulmonary venous plexus and the splanchnic plexus, both of which originally drain into the cardinal venous plexus. Although the anomalies described above are embryologically slightly different, they all have one feature in common—the anomalous systemic supply of the lungs. Although 2 patients had congenital heart disease, it did not seem to be related to the abnormal pulmonary vasculature observed in these patients.

Anomalous drainage of the right lung into the inferior vena cava is a persistent communication between the pulmonary plexus and the primitive posthepatic vena cava. Neill *et al.*[17] felt that this anomaly was the result of an abnormal development of the right lung bud and that it was a more primitive type of malformation than the usual anomalies of the pulmonary venous return. These malformations may be associated with an aberrant systemic arterial supply, such as persisting branches of the splanchnic plexus from the dorsal aortae. The following 4 features characteristic of the anomaly have been described:[9,22,26] (1) Hypoplasia of the right lung with subsequent dextroposition of the mediastinal structures into the right hemithorax; (2) hypoplasia of the right pulmonary artery; (3) anomalous systemic supply of the right lower lobe by the abdominal aorta or its branches; and (4) anomalous venous drainage of the right lung into the inferior vena cava just below or above the right hemidiaphragm. All these features except the anomalous systemic arterial supply can be

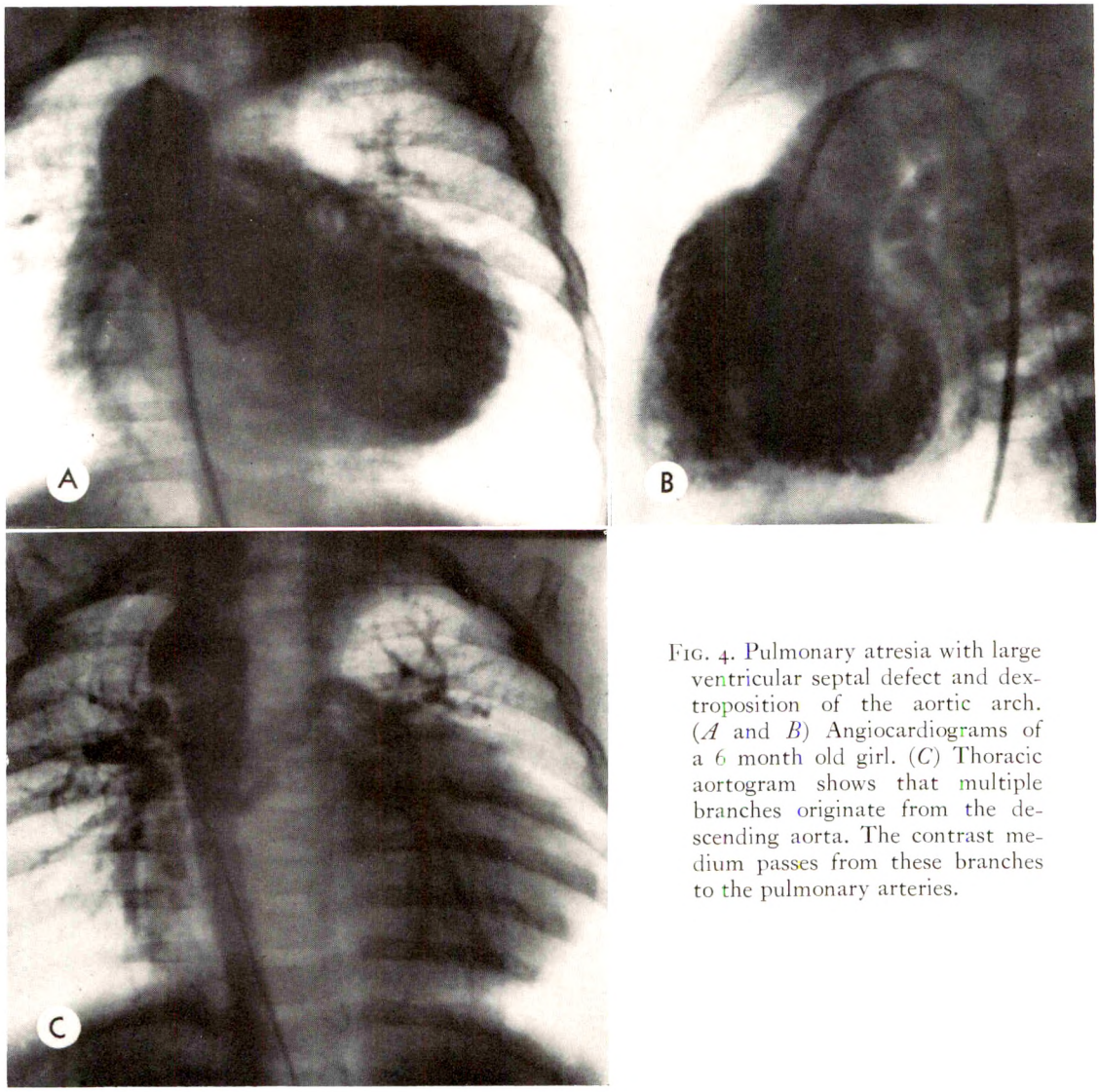


FIG. 4. Pulmonary atresia with large ventricular septal defect and dextroposition of the aortic arch. (*A* and *B*) Angiocardiograms of a 6 month old girl. (*C*) Thoracic aortogram shows that multiple branches originate from the descending aorta. The contrast medium passes from these branches to the pulmonary arteries.

detected by plain roentgenography and tomography of the chest.

Angiography is the method of choice to define the precise anatomy of the pulmonary circulation.[5] Although a systemic arterial supply may be revealed in the aortic phase of angiocardiography,[9,11,20,26] in which it was observed in 2 of our patients, the anomaly may be missed owing to insufficient density of the contrast medium in the arteries and to superimposition of adjacent structures. Thoracic aortography can disclose the origin, course and distribution of the anomalous vessels.

Despite the absence of reports in the literature, selective angiography must be regarded as preferable, because it allows examination not only of the arteries, but also of the veins (Fig. 1). In a patient with hypoplasia of the right pulmonary artery, the mediastinal structures are displaced to the right. It is therefore often not possible to decide whether one part of the right lung is supplied from another source, *i.e.*, the systemic circulation. Furthermore, patients with this syndrome often have recurrent hemoptysis, recurrent infection and cardiac decompensation. Such patients are

therefore subjected to explorative thoracotomy and, if indicated, the entire right lung or the right lower lobe is removed. In such cases preoperative demonstration of the anomalous systemic supply is invaluable.

Absence of one pulmonary artery is another type of malformation seen in association with pulmonary anomalies. While absence of the left pulmonary artery is frequently accompanied by cardiac malformations, most patients without a right pulmonary artery have a normal heart.[4,28] All patients with this anomaly should, however, be examined with angiocardiography for cardiovascular malformations. The roentgenographic appearance of acquired pulmonary lesions may resemble that of hypoplasia of the right lung. The case history and bronchography may be helpful in the differentiation between these conditions.[16] A systemic arterial supply from sources other than the bronchial arteries can be demonstrated in the late phase of angiocardiography.[15] In our patients the anomalous circulation including the venous drainage was demonstrated in detail at selective angiography (Fig. 2). It could be seen from the angiograms, obtained in our

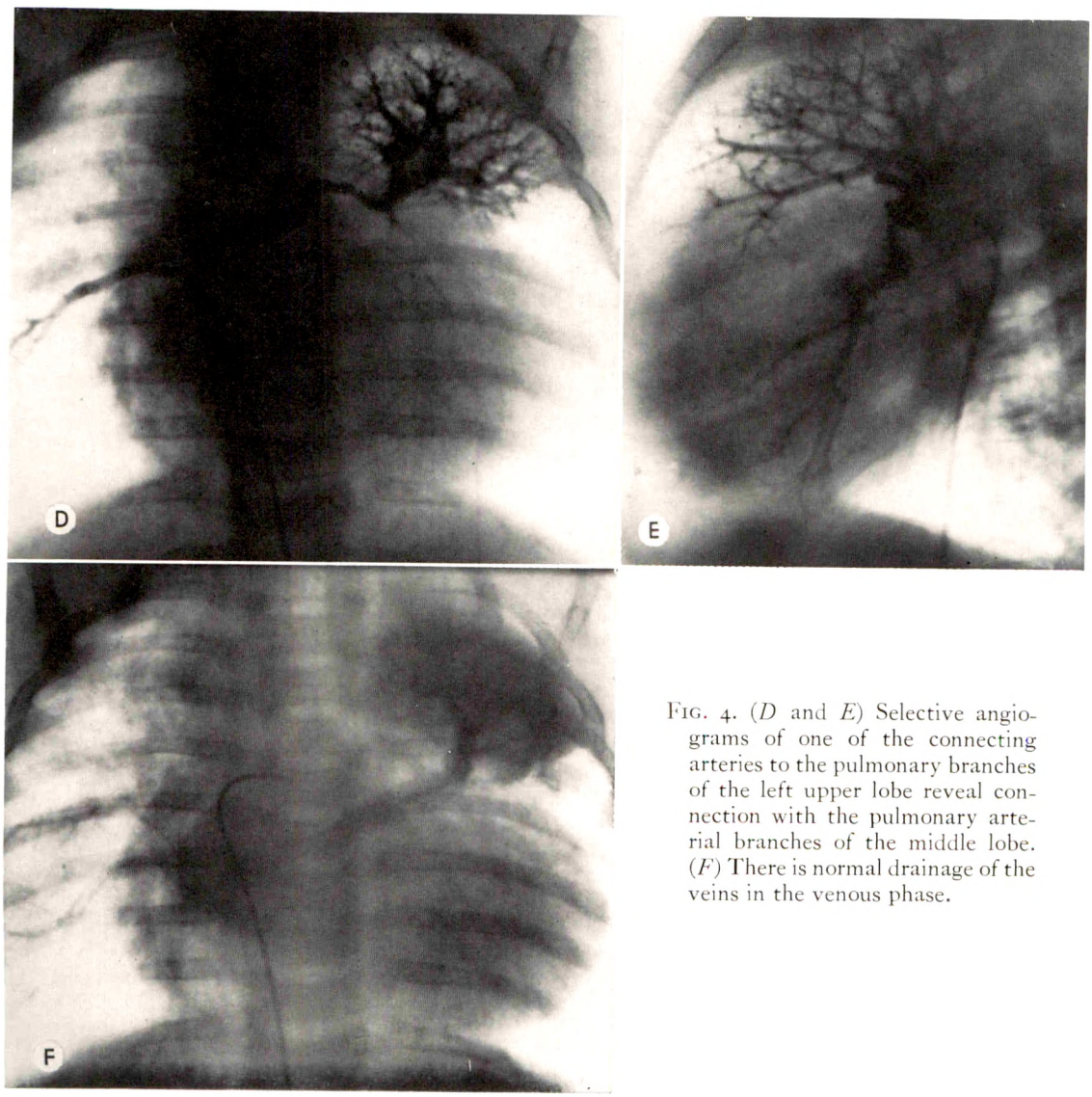


Fig. 4. (*D* and *E*) Selective angiograms of one of the connecting arteries to the pulmonary branches of the left upper lobe reveal connection with the pulmonary arterial branches of the middle lobe. (*F*) There is normal drainage of the veins in the venous phase.

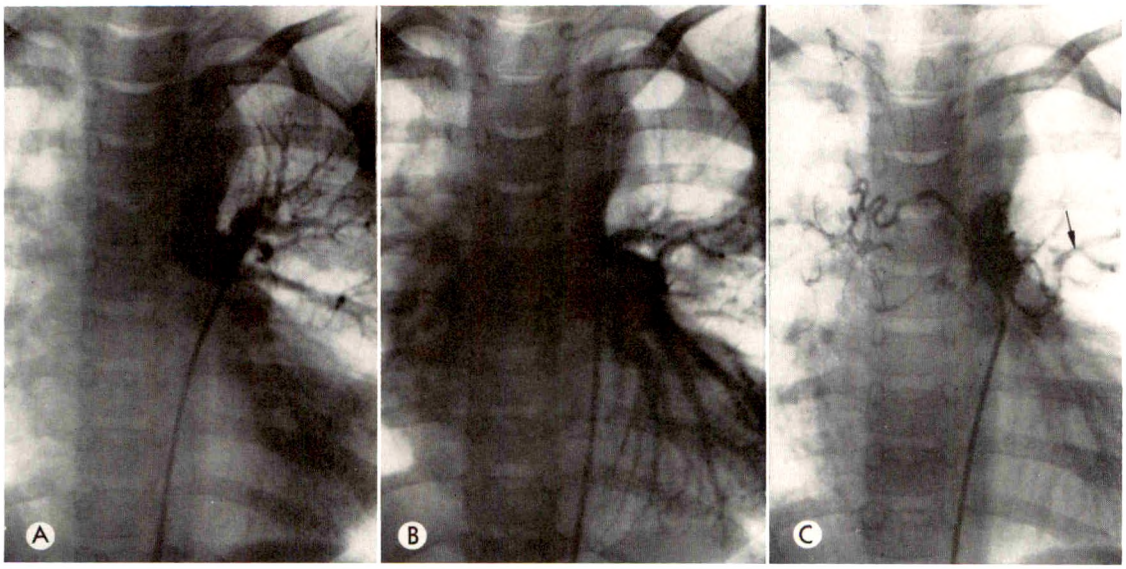


FIG. 5. Pulmonary atresia with ventricular septal defect in 4 year old girl. (*A* and *B*) Selective angiograms of the pulmonary arteries to the left lung demonstrate that the artery supplying the upper and the one supplying the lower lobe communicate with the descending aorta at different levels. (*C*) Selective bronchial angiogram shows that contrast medium passes to the branches of the pulmonary arteries (→).

patients with aplasia of the right pulmonary artery, that this anomaly is fundamentally similar to intralobar sequestration of the lung, but the presence of the right bronchial tree, although anomalous, proved that it was not a complete sequestration.

Angiography is valuable for differentiating space-occupying lesions of the lower lobe, especially of the left lung. Although the anomalous artery arising from the distal part of the thoracic aorta may be demonstrated with tomography,[10,15,27] thoracic aortography can reveal better the origin and course of the artery.[2,12,13,14,18,21,23,30] As pointed out by Wellauer[32] and observed by us in a patient not reported here, thoracic aortography may, however, fail to demonstrate the aberrant artery. On the other hand, at selective angiography, the arterial supply as well as the venous drainage of the lesion can be demonstrated, enabling distinction between intra- and extra-lobar sequestration.[1,24,25]

Patients with an extreme type of tetralogy of Fallot or with atresia of the pulmonary valve with ventricular septal defect should be distinguished from those with truncus arteriosus, because surgical correction is not indicated in the latter. According to Campbell and Deuchar[3] and Ongley *et al.*,[19] development of collaterals might cause a continuous murmur in cyanotic congenital heart disease. These two conditions can be distinguished from one another at angiocardiography and thoracic aortography. Stewart *et al.*[29] and Ongley *et al.*[19] used angiocardiography to demonstrate the bronchopulmonary anastomoses similar to those in our cases described above. It is well known that the precapillary anastomoses between the bronchial and pulmonary arteries are well developed in cyanotic heart disease.[31] At selective bronchial angiography of patients with tetralogy of Fallot the peripheral pulmonary arterial branches are filled with contrast medium via these multiple but small anastomoses. Wide connections between the descending aorta and pulmonary arteries were, however, also demonstrated in our patients with pulmonary atresia. Selective bronchial angiography and selective angiography of these connections in the same patient leave the impression that the latter may originate

from a patent ductus arteriosus or from other congenital channels, such as those supplying a sequestrated lung. They may also be bronchial arteries with large broncho-pulmonary communications. The connections between the pulmonary artery of the left upper lobe and the right middle lobe, and between branches of the thoracic aorta and the pulmonary arteries to the remaining parts of the lungs in 1 of our patients (Fig. 4) suggest that the anomalous pulmonary supply may be still more complex than hitherto observed. Selective angiography is the method of choice for demonstrating these abnormal communications between the systemic circulation and the pulmonary arteries and is useful for differentiating a truncus arteriosus from a severe form of tetralogy of Fallot. In addition, this technique may shed light on the significance of the bronchial circulation in cyanotic heart disease.

SUMMARY

Angiographic examination of 7 patients with a systemic arterial supply of the lungs with malformation of the pulmonary circulation and of 2 patients with bronchopulmonary anastomoses and pulmonary atresia with ventricular septal defect illustrates the value of selective systemic angiography in such conditions, especially for demonstrating the origin and course of the anomalous arteries and their venous drainage.

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ARTERIOGRAPHY IN INFANTS AND CHILDREN

WITH EMPHASIS ON THE SELDINGER TECHNIQUE AND ABDOMINAL DISEASES*

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WITHIN the past decade cerebral and cardiac angiography have become widely accepted as practical and valuable techniques in pediatric diagnosis. Only a few reports, however, have indicated the value of arteriography in abdominal and extremity diseases in childhood.[2,4,5,7,8] Although widely used in adults, the Seldinger technique of percutaneous catheter insertion has only occasionally been applied to children.[1,6,8,13,14] This report will describe the techniques, risks, and results of abdominal and extremity arteriography in infants and children, using mainly the Seldinger technique. It is based on 131 examinations performed at the Children's Hospital Medical Center and the Massachusetts General Hospital in the past 5 years; in 107 cases the Seldinger technique was used.

CLINICAL MATERIAL

Children of all ages were studied. The age distribution of the patients was fairly even (Fig. 1). Among the 131 patients were 4 newborns 1 or 2 days old, 8 other infants less than 6 months old, and 9 further cases less than 2 years old.

The indications for examination varied widely. Some children needed proof or delineation of abdominal masses, often within the liver. Other common indications for examination were systemic hypertension and portal hypertension. A complete list of the conditions studied is given in Table 1. All cases in Table 1 were proven by autopsy, biopsy, or surgery except where otherwise stated. The total is greater than 131 because some patients had more than 1 abnormality and because a few of the conditions are listed under 2 categories.

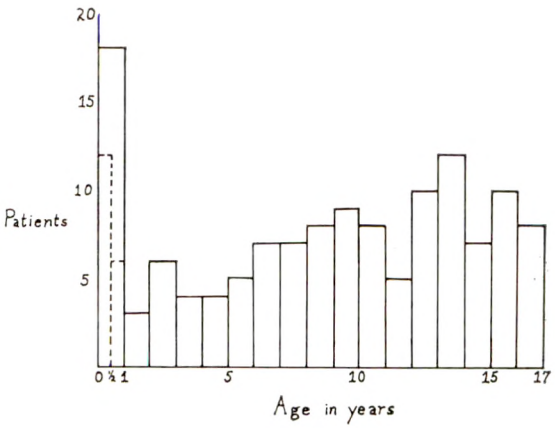


FIG. 1. Age distribution of patients studied.

TECHNIQUE

Sedation only was employed in 122 cases, usually with an intramuscular injection of demerol, phenergan, and thorazine.* Local anesthesia was used at the puncture site. Nine cases were examined under general anesthesia; however, general anesthesia was rarely used later in the series, even in infants.

The Seldinger percutaneous technique was usually employed. Our recent practice is to attempt the percutaneous approach in all infants and children after closure of the umbilical artery, which occurs at about 5 days of age. Seldinger puncture has been achieved as early as 7 weeks of age. In the entire series there were 107 successful per-

* 1 cc. of this mixture contains 6.25 mg. phenergan, 6.25 mg. thorazine, and 25 mg. demerol; 1 cc. is given for each 15 kg. of body weight, but not more than 2 cc. Children weighing more than 40 kg. were sedated with demerol and nembutal.

* Presented at the Sixty-ninth Annual Meeting of the American Roentgen Ray Society, New Orleans, Louisiana, October 1–4, 1968.
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TABLE I

CONDITIONS STUDIED IN 131 PATIENTS*

I. Liver masses	22
Hepatoma (includes hepatoblastoma)	6
Metastasis	6
Hamartoma	2
Liver abscess	2
Extrinsic mass	2
Hemangioma	1
Calcified hematoma	1
Unbiopsied mass	2
II. Other liver conditions	11
Radiation hepatitis	4
Cirrhosis	4
Budd-Chiari syndrome	2
Biliary atresia	1
III. Portal hypertension	14
Cirrhosis	8
Portal vein thrombosis	4
Budd-Chiari syndrome	2
Portosystemic shunts evaluated for patency	8
IV. Renal diseases, excluding hypertension	25
Renal agenesis	3
Renal trauma	3
Renal transplant	3
Wilms' tumor	3
Bilateral multicystic dysplastic kidneys	2
Pyelonephritis without hypertension	2
Hydronephrosis	2
Hypoplasia with pyelonephritis	1
Pelvic kidney	1
Papillary renal cell carcinoma	1
Polycystic kidneys	1
Vascular obstruction of an infundibulum	1
Acute tubular necrosis	1
Hamartoma in tuberous sclerosis (unproven)	1
V. Arterial hypertension	22
Pyelonephritis (4 not histologically proven)	8
Glomerulonephritis	3
Renal artery stenosis	2
Abdomen coarctation	2
Renal infarct	1
Pheochromocytoma	1
Negative study	5
VI. Adrenal tumors	4
Neuroblastoma	2
Adrenocortical carcinoma	1
Pheochromocytoma	1
VII. Extremity diseases	13
Arteriovenous malformation	2
Lymphangio-hemangioma (no arteriographic findings)	2
Arterial thrombosis	2
Osteogenic sarcoma	2
Giant mixed hemangioma	1
Reticulum cell sarcoma	1
Osteochondroma obstructing popliteal vein	1
Arteritis (unproven)	1
False aneurysm	1
VIII. Miscellaneous diseases	8
Retroperitoneal ganglioneuroma	2
Duodenal hematoma	1
Pancreatic insulinoma	1
Sacrococcygeal teratoma	1
Lymphangio-hemangioma of retroperitoneum	1
Hemangioma of face	1
Bowel hemangioma	1
IX. Negative studies	25
Clinically suspected renal or adrenal masses (exploration confirmed absence of tumor)	5
Hypertension, no cause found	5
Gastrointestinal bleeding, no source found	3
Hematuria, no cause determined	3
Lymphangio-hemangioma, without arteriographic abnormalities	3
Post-radiation malabsorption	2
Abdominal pain	1
Suspected liver mass (false positive interpretation, negative exploration)	1
Bronchogenic cyst	1
Mediastinal mass, never biopsied	1

* Arteriogram positive except where indicated. All cases proven unless otherwise indicated. Some examinations listed under two different headings.

cutaneous punctures using the Seldinger technique of catheter insertion, 18 approaches by cutdown with insertion of the catheter after needle puncture or arteriotomy, 4 umbilical artery catheterizations in newborns 1 or 2 days old, and 2 needle punctures without catheter insertion for femoral or popliteal studies. In only 3 cases

was percutaneous puncture unsuccessful. Cutdown was performed as the primary procedure in small children early in the series but later was reserved for the infrequent patient in whom percutaneous puncture was unsuccessful.

Table II gives the needles, guide wires, and catheters currently used. The size of the catheter must be governed by the size of the femoral artery. Just as the legs of an infant are proportionately smaller than his head and trunk, so are the femoral arteries of infants and children relatively smaller than their aortas and brachiocephalic and major visceral arteries. Thus even smaller catheters are necessary than one would expect. Early in the series, use of catheters that were too large frequently caused arterial spasm. With smaller catheters, this has become rare.

At Children's Hospital, selective catheterization of the appropriate visceral artery was attempted even in the youngest infants if indicated; for example, when a hepatic or renal mass was suspected or if portal venous opacification was desired. At the Massachusetts General Hospital, nonselective aortography was used under the age of 2. Selective angiography can be accomplished more frequently and easily in infants and children than in adults; 106 vessels were selectively catheterized. Only 3 selective catheterization attempts failed. Superselective catheterization of hepatic and splenic arteries and catheterization of lumbar arteries were also accomplished without difficulty.

The contrast agent used was meglumine diatrizoate.* The dosage was $\frac{1}{2}$–$\frac{3}{4}$ cc. per kg. for aortography and selective celiac or superior mesenteric angiography, unless portal venous visualization was desired, when 1 cc. per kg. was used. For selective renal angiography approximately 0.1 cc. per kg. was given. (Thus, 2 cc. was used for a selective renal arteriogram in a 20 kg. child, 4 cc. in a 40 kg. child, and 7 cc. in fully grown adolescents.)

COMPLICATIONS

Complications were uncommon. Among the 107 Seldinger catheterizations were 3 cases of temporary (less than 6 hours) severe spasm with dampening or disappearance of the pulses distal to the puncture site. In 8 other patients, there was temporary slight lessening of pulse amplitude. Spasm seemed to be caused by catheters too

* Renografin 60 per cent was used in most cases.

Table II

NEEDLES, GUIDE WIRES, AND CATHETERS CURRENTLY IN USE

Age	Type of Study	Needle	Guide Wire	Catheter
1 week–1 year	Selective arteriography and aortography	19 gauge* or 20 gauge*	0.025 inch or 0.021 inch	RPX 025† or RPX 037† 0.038 inch outer diameter or 0.048 inch outer diameter
1–6 years	Selective arteriography and aortography	18 gauge*	0.035 inch	RPX 045† 0.062 inch outer diameter
6–16 years	Selective arteriography	18 gauge*	0.035 inch	Kifa red
6–16 years	Aortography	18 gauge*	0.035 inch	RPX 055† or RPX 062 0.075 or 0.082 inch outer diameter

* Thin-wall New needle,[12] manufactured by Becton-Dickinson.
† Formocath thin-wall catheters, by Becton-Dickinson.

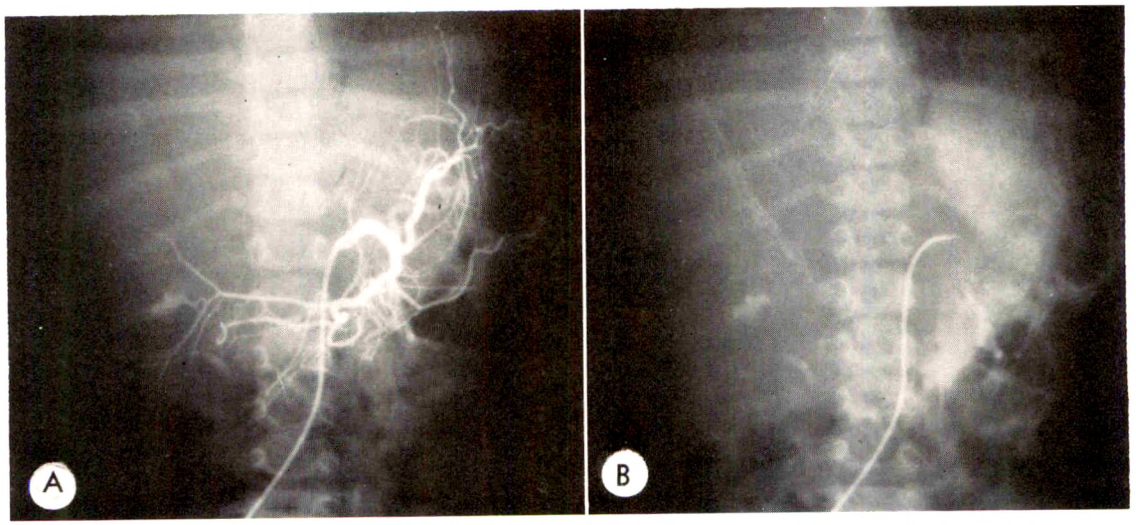


FIG. 2. *Cystic hamartoma.* This 9 month old infant presented with an abdominal mass. Angiography was performed to show the location of the mass within the liver prior to resection. A catheter was introduced by the Seldinger method from the femoral artery.

(*A*) The common hepatic artery has been selectively catheterized; except for the gastroduodenal, all vessels opacified are hepatic arteries. The left hepatic artery and its branches are displaced into the left upper quadrant but are otherwise normal. The right hepatic artery branches are displaced downward and stretched by an avascular mass within the right lobe. (*B*) Late roentgenogram shows the mass to be avascular except for a few thread-like small vessels passing obliquely through the mass.

At surgery a large cystic mass was found in the right lobe of the liver, which was resected. The multilocular cyst contained fibrous nodules, lymphatics, arteries, veins, and a few cords of liver cells within its walls.

large for the patient's femoral artery. During the later part of this series smaller thin-wall catheters were used, and spasm was uncommon except in the smallest infants.

Thrombosis was presumed if distal pulses did not return within 6 hours. This occurred after Seldinger puncture in 2 infants, aged 7 weeks and 5 months. These patients suffered no other signs or symptoms, and the temperature and color of the extremities remained normal. No treatment was necessary.

The long-term effects, if any, of catheter insertion on growth of the leg are not known. One of our examinations showed femoral occlusion in a 9 year old girl whose femoral artery had undergone arteriotomy elsewhere for exchange transfusion in the newborn period; her leg was short.

There were 11 very small hematomas in the Seldinger group. All resolved readily. In 1 hypertensive patient bleeding occurred 4 hours after the procedure, but the bleeding stopped with manual compression.

In the 18 patients who underwent surgical cutdown with arteriotomy or open needle puncture, there were 2 thromboses and 1 mild spasm. No hematomas were recorded in this group.

There were 2 reactions to the contrast agent. The more severe was generalized giant hives in a 2 year old child. The hives responded to parenteral antihistamine.

One patient had spontaneously remitting abdominal pain and low grade fever for 7 days after a difficult hepatic artery catheterization; the cause was never determined. A transient slight elevation of temperature occurred in a few other patients.

There were no other complications. No deaths resulted from these procedures.

RESULTS OF ANGIOGRAPHIES

Twenty-two masses affecting the liver were studied. Twenty were within the liver and 2 were extrinsic to it, but caused hepatic deformity. As in adults, arterial displacement and stretching and tumor

vessels and stain were common and helpful findings. The primary hepatic cell carcinomas (hepatomas) were the most vascular tumors and usually had large feeding arteries, numerous irregular tumor vessels, and intense tumor staining.[4,7,10] The vascularity of other tumors, such as hamartomas and metastatic lesions, was variable but usually less intense. No hepatic tumor was missed by arteriography. There was 1 false positive angiographic interpretation. Angiography was of particular value in preparation for hepatic resection. It accurately localized any mass and demonstrated its relation to the hepatic blood supply. Aberrant hepatic arteries are frequent, and their demonstration prior to hepatectomy is important[11,15] (Fig. 2, *A* and *B*).

Eleven patients with other hepatic diseases were studied. The 4 cases of cirrhosis showed corkscrewing and crowding together of vessels within a small fibrotic liver. Four cases of radiation hepatitis, which will be described in a subsequent report, had findings surprisingly similar to those of cirrhosis.

Fourteen children with portal hypertension caused by cirrhosis, portal vein thrombosis, or hepatic vein thrombosis were studied in order to visualize the portal venous system. The patency or occlusion of the portal venous system and of porto-systemic shunts was accurately demonstrated in all cases by means of selective splenic or superior mesenteric artery injections[9] (Fig. 3, *A* and *B*).

Renal lesions in general were quite accurately demonstrated by angiography. Relatively few patients with renal masses were studied by angiography. Only in bilateral renal masses, recurrences of renal neoplasm, and other complicated cases was angiography felt to be necessary. The 3 Wilms' tumors in this series were mildly or moderately hypervascular, with small tumor vessels, mild tumor staining, and little or no arteriovenous shunting.[3,8] They were much less vascular than the usual adult hypernephroma (Fig. 4, *A* and *B*).

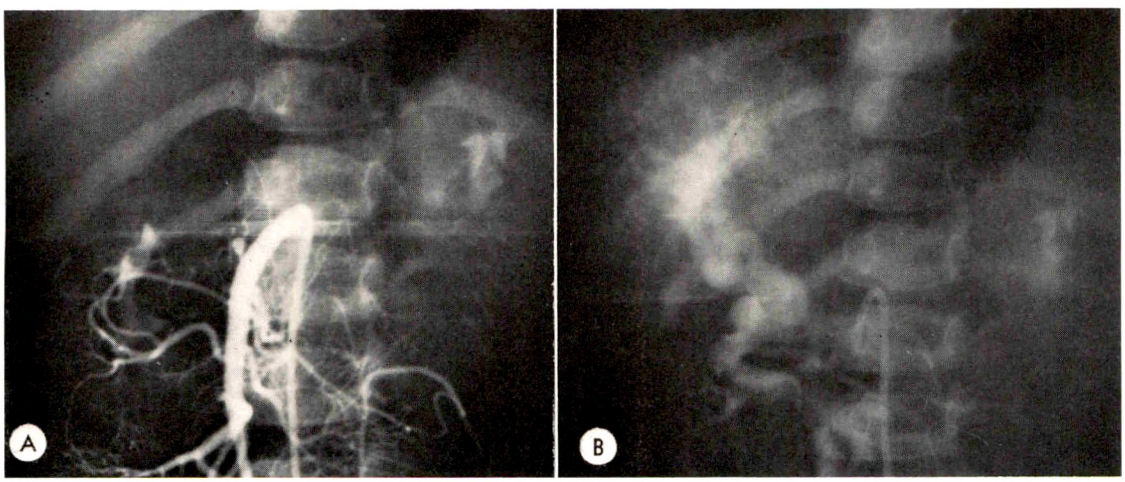


Fig. 3. *Portal vein thrombosis.* This 6 year old child had developed omphalitis as a newborn after receiving exchange transfusions through the umbilical vein. He subsequently developed portal hypertension and gastrointestinal bleeding. Angiography was performed to show the site of obstruction prior to attempting a porto-systemic shunt. Using the percutaneous Seldinger technique, the catheter has been placed in the superior mesenteric artery.

(*A*) Superior mesenteric artery injection. (*B*) The venous phase, during which the contrast material returns from the bowel wall, shows that the portal vein has been thrombosed. Several tortuous veins are seen in the porta hepatis; these represent dilated periportal collaterals and perhaps partial recanalization of the portal vein.

Portal vein thrombosis was confirmed at surgery.

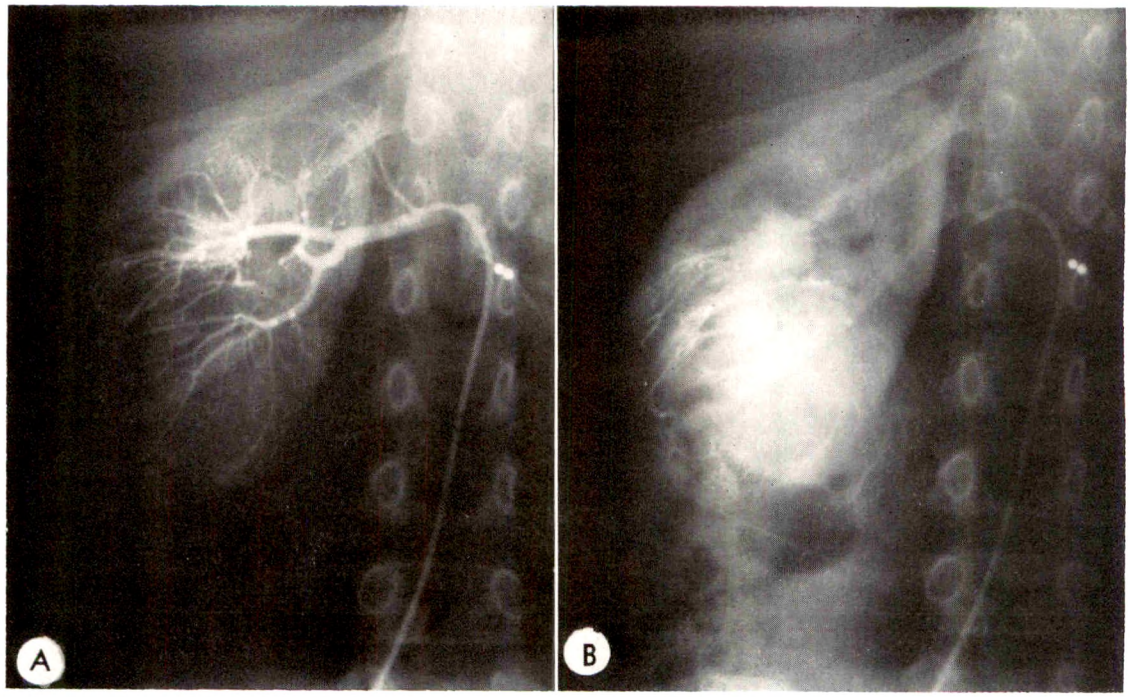


FIG. 4. *Wilms' tumor.* This febrile 8 year old girl had a mass in the lower pole of her right kidney by intravenous pyelography. Because of her age and the fever, a cortical abscess was considered. Angiography was performed to attempt further definition of the mass.

(*A*) Selective renal arteriography shows stretched and displaced vessels in the lower pole of the right kidney. (*B*) Later roentgenogram shows many small irregular tumor vessels and tumor staining. There is no arteriovenous shunting. The appearance suggests tumor rather than infection.

The kidney was resected, and a Wilms' tumor was found.

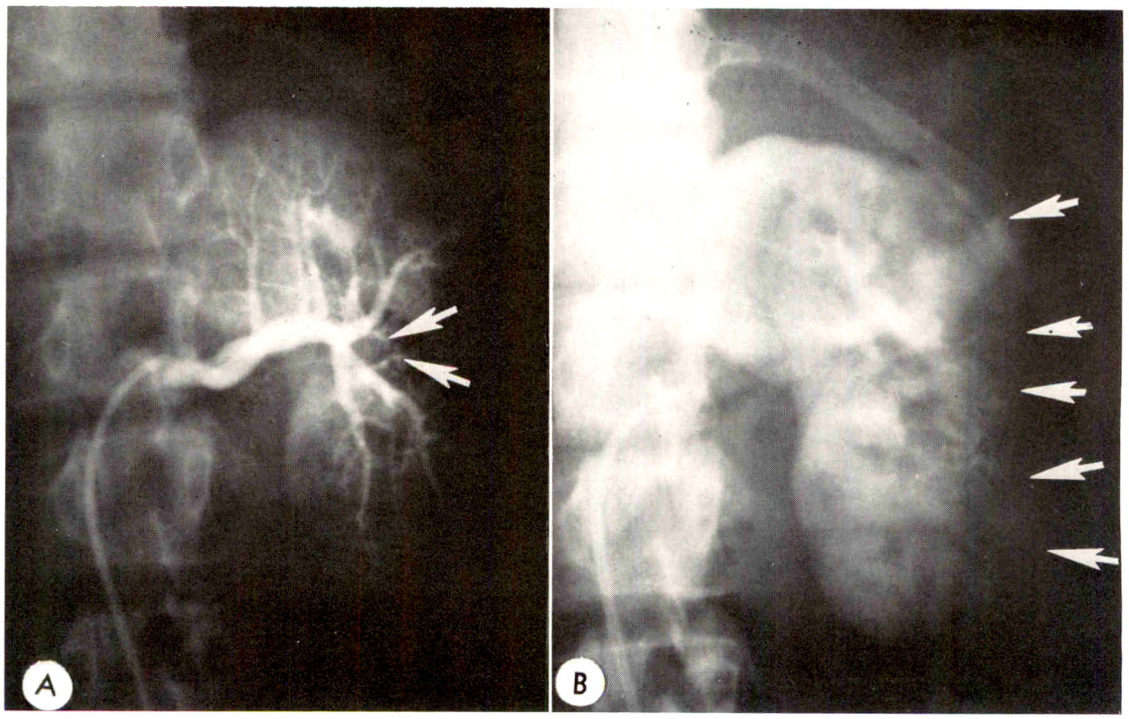


FIG. 5. *Renal infarct.* This 13 year old girl had had hypertension for 3 months. The blood pressure was 160/120. Intravenous pyelography was normal except for slight irregularity of the left kidney outline. An aortogram showed normal main renal arteries.

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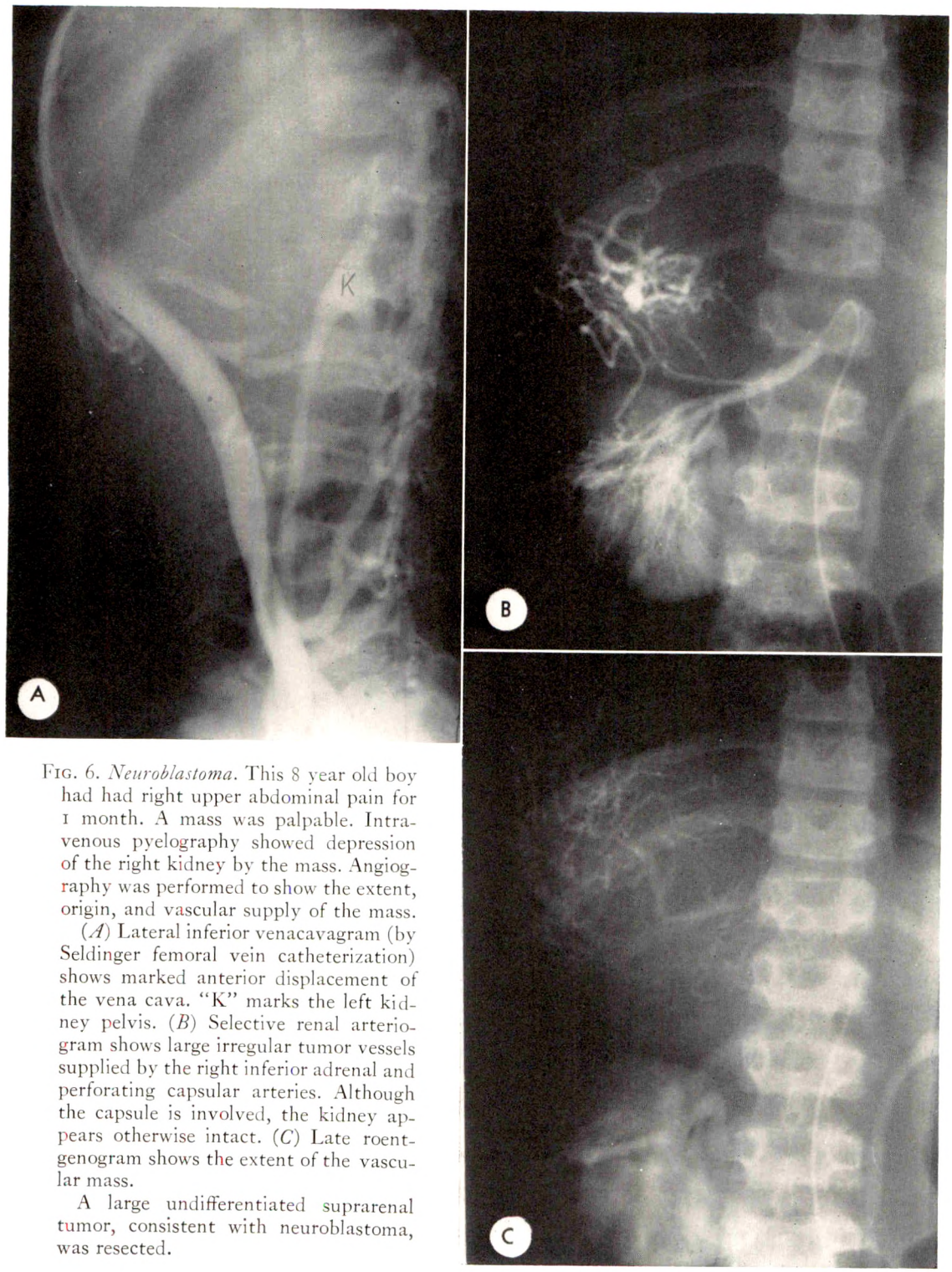


FIG. 6. *Neuroblastoma.* This 8 year old boy had had right upper abdominal pain for 1 month. A mass was palpable. Intravenous pyelography showed depression of the right kidney by the mass. Angiography was performed to show the extent, origin, and vascular supply of the mass.

(*A*) Lateral inferior venacavagram (by Seldinger femoral vein catheterization) shows marked anterior displacement of the vena cava. "K" marks the left kidney pelvis. (*B*) Selective renal arteriogram shows large irregular tumor vessels supplied by the right inferior adrenal and perforating capsular arteries. Although the capsule is involved, the kidney appears otherwise intact. (*C*) Late roentgenogram shows the extent of the vascular mass.

A large undifferentiated suprarenal tumor, consistent with neuroblastoma, was resected.

(*A*) Selective left renal arteriogram shows abrupt amputation of 2 interlobar branches (arrows) to the middle zone of the kidney. (*B*) The nephrogram shows marked thinning of the renal cortex in this region (arrows).

A nephrectomy was performed, and the blood pressure returned to normal. There were several infarcts within the resected kidney.

Twenty-two children with systemic hypertension were studied. There were 2 cases of renal artery stenosis, 2 abdominal coarctations, 1 renal infarct, and 1 pheochromocytoma. In 11 other children arteriography was abnormal and consistent with the clinical and pyelographic diagnoses of glomerulonephritis and pyelonephritis. There were 5 negative studies in children whose hypertension remained idiopathic (Fig. 5, *A* and *B*).

Four adrenal tumors were studied; all were accurately delineated by angiography. Tumor vessels and tumor staining were present in all cases (Fig. 6, *A–C*).

In 13 cases, the angiography was undertaken to demonstrate extremity lesions. The extent and nature of arteriovenous malformations and of some types of hemangioma were shown, as were the vessels supplying them. Other arterial lesions such as thrombosis, arteritis, and false aneurysms were all accurately depicted. Several neoplasms of the bones and soft tissues were delineated (Fig. 7, *A* and *B*).

Also demonstrated were 2 retroperitoneal ganglioneuromas, a retroperitoneal lymphangio-hemangioma, a sacrococcygeal teratoma, a pancreatic insulinoma, and a bleeding hemangioma of the ileum (Fig. 8, *A* and *B*; and 9, *A–E*).

There were 25 negative arteriograms (19 per cent of the entire series). Most of these were obtained because of hypertension, hematuria, or a questionable abdominal mass. The indications for angiography were kept fairly strict. Since angiography was not performed without solid indication, there was a high incidence (81 per cent) of positive examinations.

CONCLUSIONS AND SUMMARY

One hundred and thirty-one infants and children underwent arteriography of the abdomen or extremities, 107 by the Seldinger percutaneous technique; 106 visceral arteries were selectively entered, with greater ease than in adults. Complications were uncommon. There was no loss of life or limb. Two asymptomatic thromboses occurred after Seldinger catheterization; they did not require treatment. There were no significant hematomas.

Various modifications of technique which we have found helpful are described.

Angiography was particularly useful in preparation for hepatic resection, for it accurately localized any mass, showed its relationship to the blood supply, and demonstrated the operatively important variations in the origins of the hepatic arteries. In portal hypertension the portal venous system was accurately shown in all cases. Precise demonstration of patency or thrombosis of shunts was attained. Angiography was abnormal in 17 of 22 cases of systemic hypertension. It was useful in a great many other conditions (Table 1).

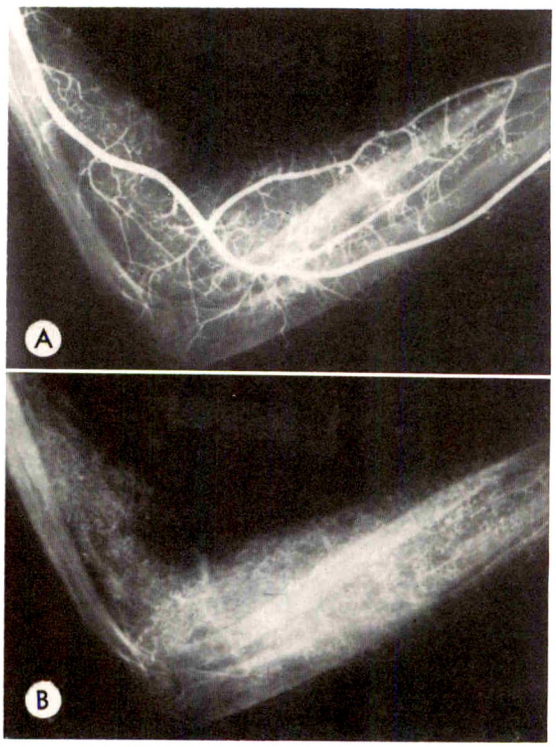


FIG. 7. *Giant mixed hemangioma.* This 10 year old boy had lobular masses within his enlarged, discolored, painful left arm. A femoral catheter introduced by the Seldinger method was selectively placed in the left subclavian artery.

(*A*) The arterial phase shows displacement of the brachial, ulnar, and radial arteries by large vascular masses. (*B*) The extreme vascularity of the masses is shown in later roentgenograms.

Biopsy showed a giant mixed hemangioma.

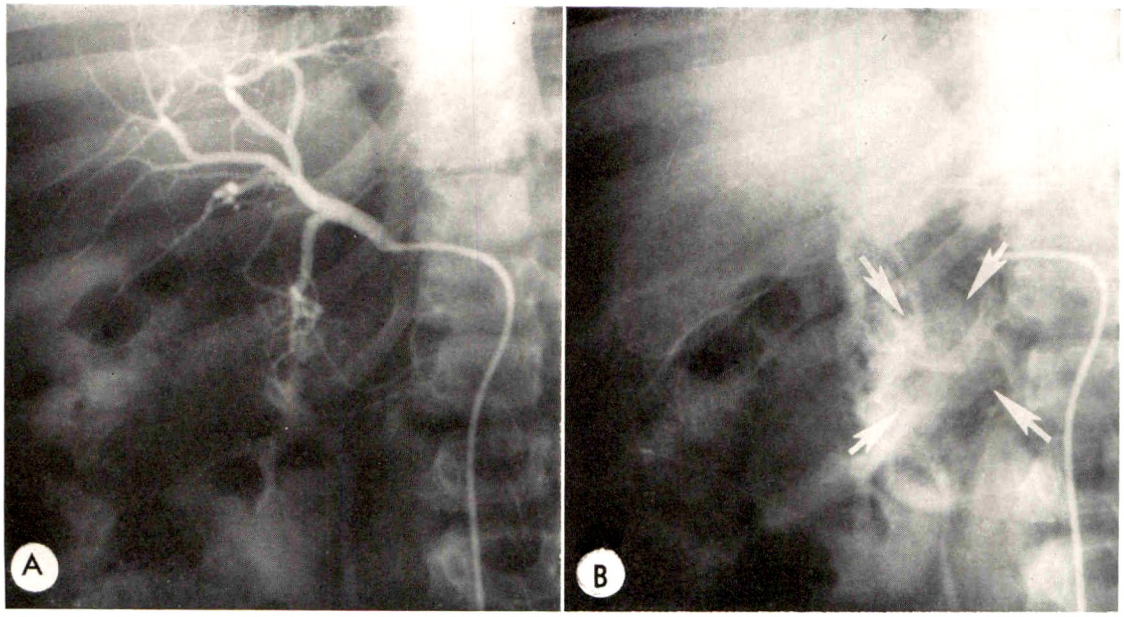


FIG. 8. *Pancreatic insulinoma.* A 12 year old boy had had worsening seizures for 3 months. Severe hypoglycemia was discovered during one of these seizures. Angiography was performed in an attempt to locate the suspected pancreatic islet cell adenoma.

(*A*) A selective hepatic arteriogram shows a few small abnormal arteries arising from the retroduodenal artery. (*B*) A stain is seen in the region of the head of the pancreas (arrows).

A 3 cm. pancreatic insulinoma was removed.

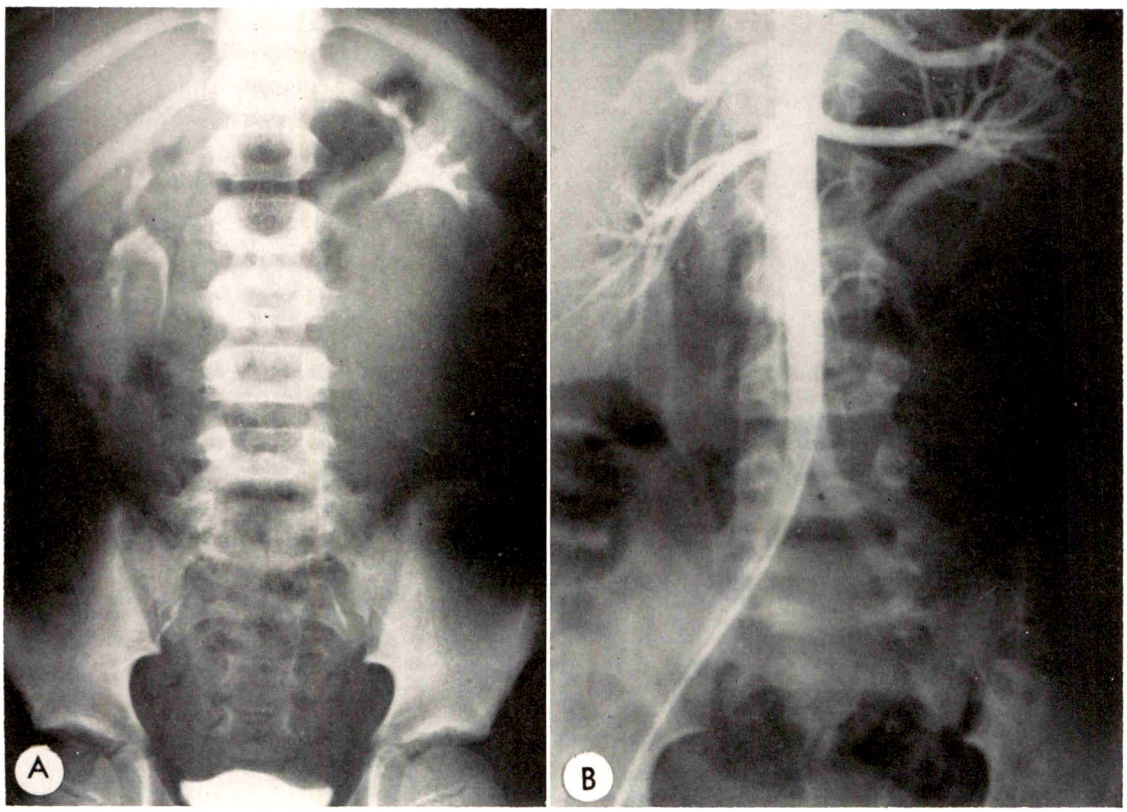
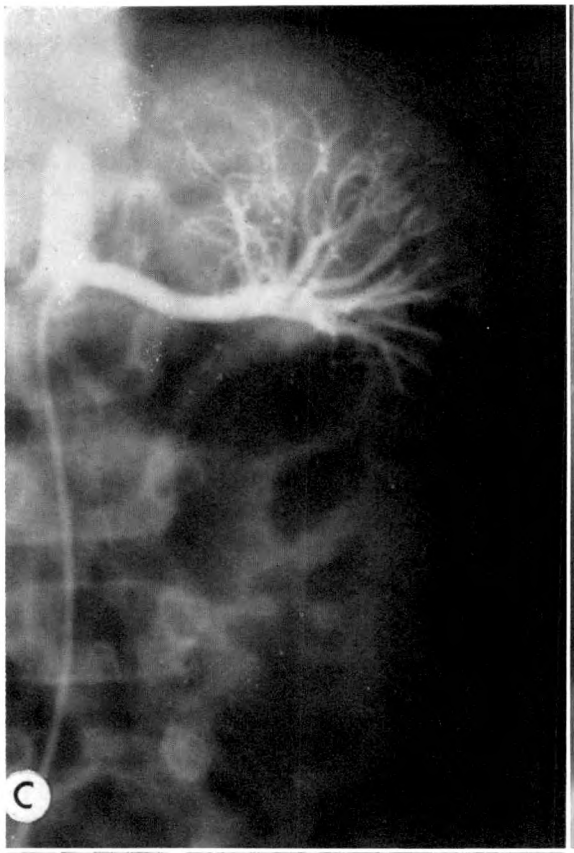
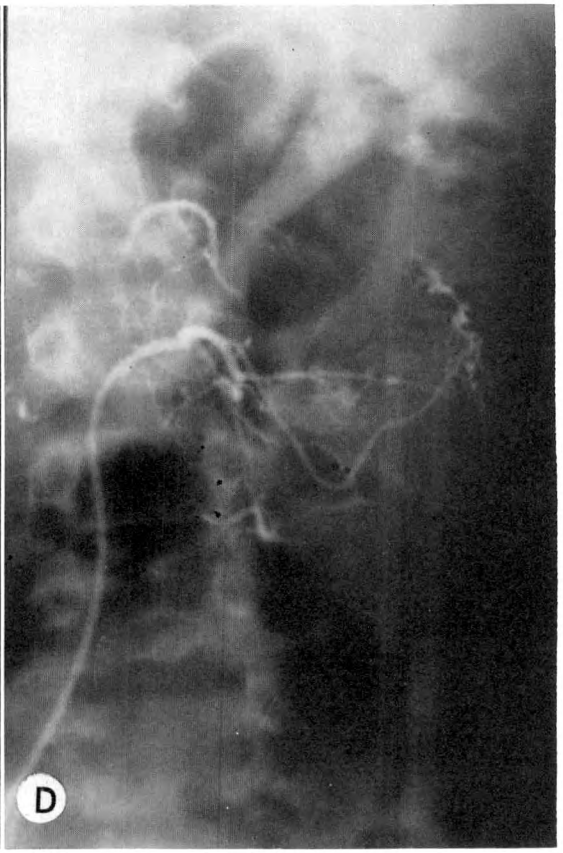


FIG. 9. *Ganglioneuroma.* Eight days prior to angiography, this 7 year old boy had fallen and injured his left side. (*A*) Intravenous pyelogram shows elevation and lateral displacement of the lower pole of the left kidney. A rim of calcification is seen in the lower portion of the infrarenal mass. (*B*) The aortogram shows slight displacement of the aorta to the right.





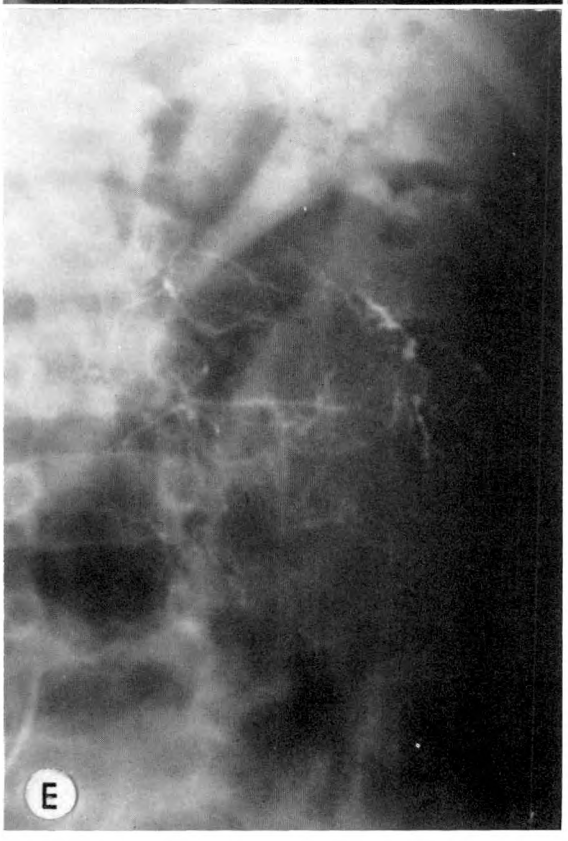


FIG. 9. (*C*) The selective left renal arteriogram shows the kidney to be intact although displaced. (*D*) A selective lumbar arteriogram shows enlarged branches giving rise to abnormal irregular tumor vessels within the mass. (*E*) Later roentgenogram demonstrates the numerous pathologic vessels within the tumor, which is shown to be solid rather than cystic.

A large ganglioneuroma was removed; it could be separated easily from the kidney.

Seldinger catheterization and selective arteriography are safe, diagnostically quite helpful, and usually surprisingly easy in infants and children.

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ABNORMAL LEFT KIDNEY FOLLOWING SPLENORENAL SHUNT*

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THE operative procedure involving anastomosis of the splenic vein to the left renal vein is an accepted method of reducing portal hypertension in patients with cirrhosis and bleeding esophageal varices.[3,4] A case report is presented of a 10 year old girl with portal cirrhosis found to have hematuria, proteinuria, casts, and a small left kidney 5 years after a splenorenal shunt.

REPORT OF A CASE

A 10 year old Caucasian girl was admitted to the University of Minnesota Hospitals in December 1967 because of jaundice, edema of the lower extremities, and increasing abdominal girth over the previous 2 months.

Admission No. 1. She had been first admitted at 1 month of age because of persistent obstructive jaundice since birth. Physical examination at that time revealed a 3.5 kg. icteric infant with a single spider angioma on the back. The blood pressure was 68 in the upper extremities by flush method. The liver edge was palpable at 4 cm. below the right costal margin. The spleen tip was barely palpable. The urinalysis was normal except for the high amount of qualitative bilirubin. The serum bilirubin was 4.3/7.4 mg. per cent on admission and dropped to 1.3/2.0 mg. per cent during her hospital course. She was discharged with no definite diagnosis.

Admission No. 2. The patient returned to the hospital at 6 months of age because of hematemesis. Her weight at that time was 6 kg. The liver was palpable 5 cm. below the right costal margin. Prominent subcutaneous abdominal venous collaterals were present. The urinalysis was normal. The bilirubin was 0.4/1.0 mg. per cent. The alkaline phosphatase was 82 King-Armstrong units. An upper gastrointestinal series did not demonstrate varices. No further bleeding occurred and she was discharged.

Admission No. 3. She was admitted for further evaluation at 3 years of age. The blood pressure was 120/60. Hepatomegaly and mild icterus were present. Occasional blood cells were noted on routine urinalysis, and a 12 hour Addis count contained 1,135,000 red blood cells, 89,000 white blood cells and no protein. A urine culture was not obtained. The serum bilirubin was 1.4/3.8 mg. per cent, alkaline phosphatase 91 King-Armstrong units, and SGOT 173 International Units. An upper gastrointestinal series demonstrated esophageal varices.

Admission No. 4. She returned to the hospital at the age of 5 years because of two bouts of hematemesis. Physical examination findings included icterus, necrotic appearing teeth, and massive hepatosplenomegaly. An intravenous pyelogram showed both normal sized kidneys and normal collecting systems (Fig. 1). The bil-



FIG. 1. A 15 minute intravenous pyelogram made on December 11, 1962, when the patient was 5 years old. Both kidneys are of normal size and contour. The left kidney measures 10.4 cm. in length, which is slightly more than 1 standard deviation above the mean.[2]

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irubin was 1.8/3.9 mg. per cent, alkaline phosphatase 97 King-Armstrong units, and bromsulphalein retention 26 per cent. The urinalysis was negative for sugar, albumin, cells, and casts. Urine culture was sterile. A splenoportogram demonstrated enlarged splenic and portal veins. The splenic pulp pressure was 330 mm. saline. In view of the demonstrated varices, the markedly elevated portal pressure, and the repeated bouts of hematemesis, it was decided that a splenorenal shunt and splenectomy should be performed. At operation, the common bile duct was found to be of normal size. The splenic vein was approximately 1 cm. in diameter. The liver was grossly cirrhotic with a hard nodular surface. Following completion of the venous anastomosis, the proximal portion of the renal vein was found to be distended and tense to palpation. The anastomosis, therefore, was taken down and the shunt reformed. At the termination of the procedure good flow was present both in the splenic and renal veins. Portal pressure was reduced to 150 mm. of saline. Urinalysis at this time was negative for blood cells and protein.

Four months later the patient was seen because of daily temperature spikes of 103° to 104° F. A catheterized urine culture grew out greater than 100,000 *Paracolobactrum coliforme* species and she was treated for 2 weeks with sulfisoxazole. The urine culture was sterile 5 months later. The patient then moved to California and was not seen here again until December 1967.

Admission No. 5. She entered the hospital once again because of edema. Over the preceding month this had responded somewhat to treatment with hydrodiuril. There was no history of nausea, vomiting, hematemesis, or melena. She occasionally complained of vague right flank pain without dysuria or gross hematuria. Physical examination revealed an alert, undernourished, edematous, icteric 10 year old girl. The blood pressure was 120/76, pulse 90 per minute, and respirations 18 per minute. The oral temperature was 100° F. Several large spider angiomas were present on her back. There was palmar erythema and marked clubbing of fingers and toes. Her teeth were in a poor state of repair and blackish stained because of prolonged iron intake. The lungs were clear to auscultation. A Grade 2 over 6 systolic murmur was heard best over the aortic region and radiated to both carotid arteries. A fluid wave was present in a soft, symmetrically protuberant abdomen. A hard nodular left lobe of the liver was palpable 3 cm. below the xyphoid process. The neurologic examination was within normal limits. The hemoglobin was 12.3 gm. per cent. The white blood cell count was 12,200 per cubic mm., with a normal differential. The platelets were 238,000 per cubic mm., and the sedimentation rate 94 mm. per 60 minutes. Prothrombin time was 12.9 seconds and partial thromboplastin time 64 seconds, both values being well within the normal range of our hospital laboratories. The bilirubin was 2.1/4.0 mg. per cent, ornithine carbamoyl transferase 118 deca units per liter, bromsulphalein 42 per cent, serum cholesterol 633 mg. per cent, alkaline phosphatase 177 King-Armstrong units, and total serum proteins 4.5 gm. per cent (with 1.3 gm. per cent albumin and 3.2 gm. per cent globulin). The urinalysis showed 2+ red blood cells and 1+ protein. An Addis count of a 12 hour specimen revealed 224,400,000 red blood cells, 12,000,000 white blood cells, and 133,000 casts. The protein excretion was 0.1 gm. in 12 hours. A noncatheterized urine culture was sterile. The serum creatinine was 0.7 mg. per cent and blood urea nitrogen 13 mg. per cent. Creatinine clearance was 55 ml./min./1.73 m.^{2}. Intravenous pyelography and laminagraphy (Fig. 2, *A* and *B*) showed that the left kidney was small and the cortex atrophic in the midportion, while the right kidney was hypertrophic. Function was grossly normal in both, but excretion was delayed on the left side. The right kidney was sharply visualized on renal scanning and was within upper limits of normal in size and shape. The left kidney was small but showed good uptake. A renogram (Fig. 3) showed the right kidney to be normal and the left kidney smaller in magnitude, suggesting less parenchyma on the left side. A voiding cystourethrogram was completely normal with no evidence of urethral obstruction or ureteral reflux. Hepatic wedge pressure obtained via right heart catheterization was 16 mm. Hg. Left renal venography and left renal arteriography were done to determine if any occlusion was present in either the venous or arterial system (Fig. 4; 5; and 6). The left renal vein was completely patent, as was the entire shunt, with no evidence of thrombosis. Because of the absence of ureteral reflux, contraction of the parenchyma, and localized thinning of cortex (Fig. 2, *A* and *B*), the possibility of an infarction of the left upper pole was considered.

The ascites responded well to treatment with

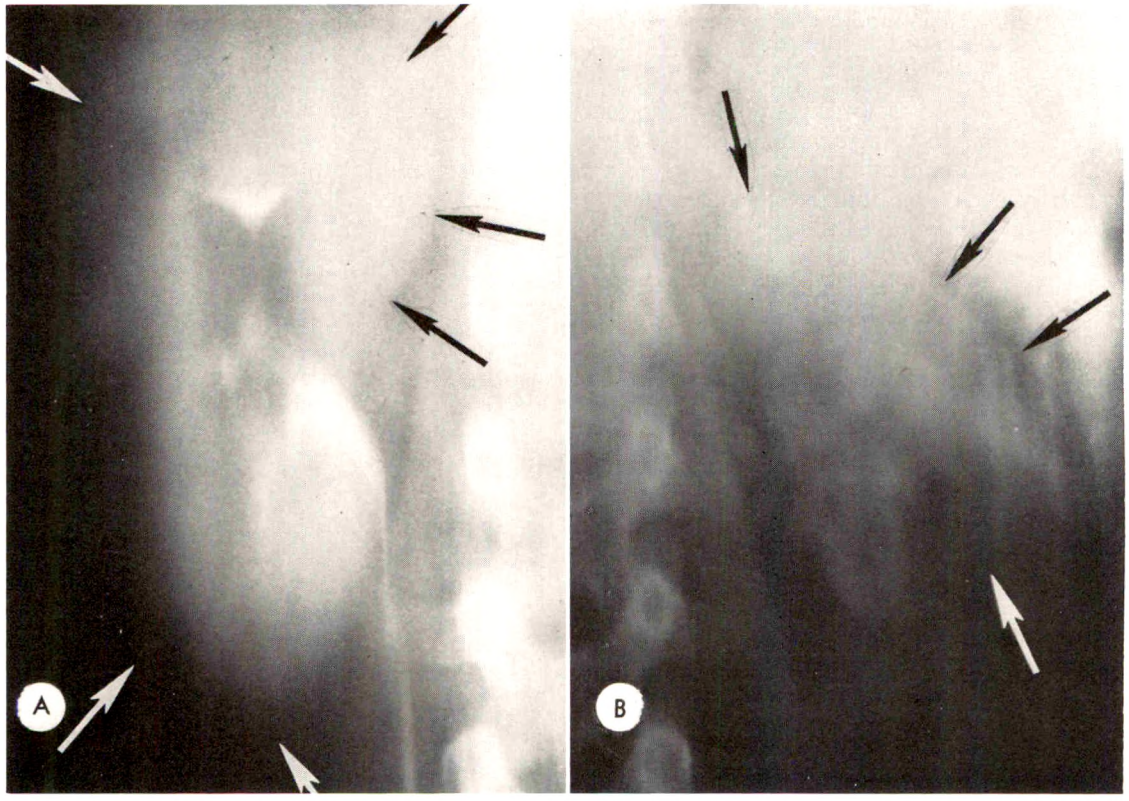


Fig. 2. A composite of (*A*) an intravenous pyelogram of the right kidney and (*B*) a laminagram of the left kidney taken 5 years following splenorenal shunt. The right kidney is hypertrophied. The left kidney is small, measuring 8.4 cm. in length, or 2 cm. less than it did preoperatively. Expected measurement of the left kidney for this patient at the age of 10 years would be 10-12 cm. The cortex is indented and thinned (not well seen here) at the middle black arrow.

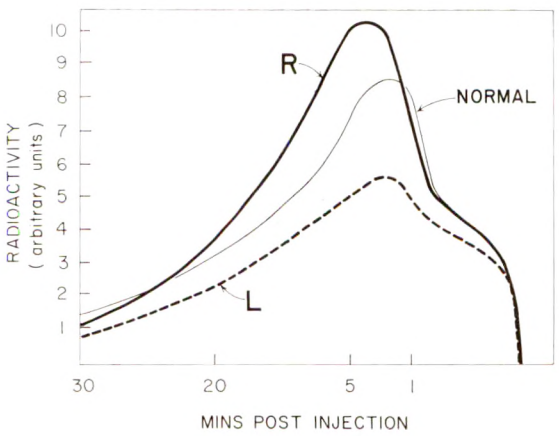


Fig. 3. A renogram done 5 years following surgery. The renogram of the right kidney is normal. That of the left kidney appears normal in shape but is considerably smaller in magnitude, suggesting less renal parenchyma on the left side.

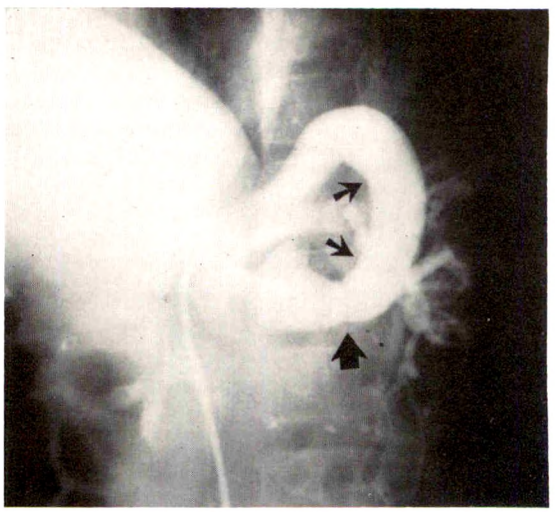


Fig. 4. Retrograde injection of the renal vein via a catheter shows a large splenic vein (smaller arrows) and a widely patent splenorenal anastomosis (large arrow).

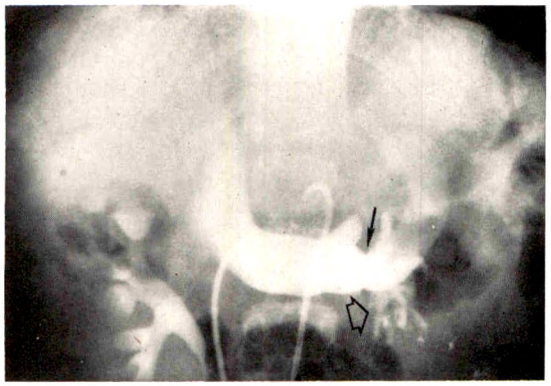


Fig. 5. Catheterization and retrograde injection of a large left renal vein demonstrate well the patent splenorenal anastomosis (solid arrow) and some reflux into relatively small peripheral renal veins (open arrow).

diuril and aldactone. During the next 5 months she had 2 urinary tract infections characterized by temperature elevations, mild right flank pain, and dysuria. Diagnosis was established by cultures of catheterized urine specimens which grew out *Escherichia coli* during the first infection and *Proteus mirabilis* 3 months later. Each organism was sensitive to ampicillin, which was the choice of treatment for both infections. She is presently being followed in the Out-Patient Clinic at the University Hospitals. Repeated urine cultures have been sterile, and she has not been taking antibiotics.*

DISCUSSION

Renal function following splenorenal shunting has not received much attention in the literature. Hivet and Gauchet[1] have noted transient hematuria and proteinuria in their adult cases as immediate postoperative findings, but renal function was said not to be permanently altered. However, postoperative intravenous pyelography was done on only 3 of their 35 patients. In reviewing 20 cases of older patients who had splenorenal shunts at the University of Minnesota Hospitals since 1958, we were unable to find evidence of renal impairment. Preoperative urinalyses were normal in all 20. Postoperative urinalyses were not obtained in 8 patients. The remaining 12 were normal. Intravenous pyelography was done preoperatively on only 3 patients and was normal. Of 3 postoperative intravenous pyelographies on 3 other patients, 2 were normal. The third showed a normal left kidney, but dilatation of the renal pelvis and calyceal blunting on the right.

The most frequently noted complication following splenorenal shunt is thrombosis of the anastomosed renal or splenic vein.[7] This apparently occurs because of the small diameters of the anastomosed veins.

It has been demonstrated in rabbits that even partial temporary renal vein obstruction can produce varying degrees of cortical and medullary necrosis of the kidney with subsequent atrophy and diffuse fibrotic changes.[8] In addition, mononuclear cell foci have been noted in the lumens of the cortical and arcuate veins.[8] Roentgenograms (Fig. 4; 5; and 6) demonstrated neither occlusion along the venous shunt pathway nor stenosis of the arterial tree. However, it may be of value to note that at



Fig. 6. Left renal arteriogram with good visualization of diffusely attenuated peripheral renal arterial branches and markedly decreased renal size, as in diffuse parenchymal disease. No major renal artery stenoses are present.

* The patient recently expired. Autopsy findings revealed a small left kidney weighing 130 gm. and 8.0 cm. in length. There were several areas of focal scarring and cortical thinning in the left renal cortex. The left renal artery circumference was 1 cm. and the right was 1.3 cm. There was no evidence of thrombosis along the entire venous shunt pathway or arterial supply. Microscopic sections ruled out evidence of pyelonephritis or glomerular lesions.

operation the initial anastomosis was taken down because of elevated pressure in the proximal portion of the left renal vein. Following re-anastomosis we know that the portal pressure was still elevated, although reduced from 330 to 110 mm. saline. With evidence of continuous elevated retrograde pressure to the left kidney we can assume a persistent increased left renal venous pressure. This may have produced in the patient a permanent diminution in rate of blood flow through the left kidney. This factor, combined with parenchymal engorgement resulting from a patent arterial supply, may be responsible for the renal atrophy. Other possibilities include renal arterial ischemia during surgery or an indolent infection which we have not been able to document.

It is well known that alterations occur in glomeruli of adults with hepatic disease,[6] and it has recently been shown that similar changes are present in kidneys of infants and children with cirrhosis. These changes consist of mesangial hypercellularity and deposition of periodic acid-Schiff positive material in the mesangium and basement membranes.[5] Whether such glomerular lesions are present in the left kidney or both kidneys of our patient is not known. Kidney biopsy has not yet been performed on this patient, but will be done in the future when her clinical condition warrants this knowledge. We also hesitate, because of the recent urinary tract infections, to insert bilateral ureteral catheters for comparative clearance studies.

CONCLUSIONS

The precise pathogenesis of the shrinkage of the left kidney in this patient is obscure. We suspect that the kidney abnormalities observed in this case may occur more often than is realized. At present there are no long term follow-up renal studies on groups of patients who have had splenorenal shunts. It would be worthwhile, therefore, to evaluate renal function in candidates for this procedure, and to repeat such studies at varying postoperative intervals.

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THROMBUS CALCIFICATION IN THE INFERIOR VENA CAVA*

A SPECIFIC ROENTGENOLOGIC ENTITY

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IN 1961, Singleton and Rosenberg[7] described 2 cases of intra-abdominal calcification in children which proved to be calcification in the thrombi of the inferior vena cava. In a review of the world's literature, these remain the only 2 proven cases of this entity. While the subject of thrombosis of the inferior vena cava has been well documented in the pediatric and pathology literature,[1–5] only brief mention has been made of this rather specific roentgenologic entity in the radiologic literature, and for this reason we present the following material.

REPORT OF CASES

CASE I. A premature male infant with a poor cry, cyanosis, an enlarged spleen and decreased breath sounds in the right lung was born in December, 1962. He was immediately given oxygen and penicillin therapy. On the fifth postpartum day the infant became jaundiced with a serum bilirubin of 16.5 mg. per cent. The hemoglobin was 15.9 gm. per cent. The child's weight which had been 4 pounds, 3 ounces dropped to 3 pounds, 11 ounces and remained at this level for the next 9 days until he slowly began to gain.

Three weeks after birth the liver edge was palpable 4 cm. below the costal margin and the spleen remained enlarged. The serum bilirubin rose to 22 mg. per cent then dropped rapidly to 10 mg. per cent during the next 4 days. At this time the hyperbilirubinemia was thought to be due to congenital atresia of the hepatic ducts. Diagnoses of galactosemia and cytomegalic inclusion disease were also entertained at this point. A liver biopsy was performed and was thought to indicate neonatal hepatitis. In view of the persistent hyperbilirubinemia, slow weight gain and enlarged spleen and liver, the patient was transferred to The Children's Hospital of Philadelphia at about $2\frac{1}{2}$ months of age. Roentgenograms of the abdomen at this time revealed a bullet-shaped calcification adjacent to the spine on the right side just below the diaphragm (Fig. 1*A*). An inferior venacavagram revealed complete obstruction of the inferior vena cava at the level of the calcification (Fig. 1, *B* and *C*). Due to the child's clinical course and calcification in the inferior vena cava, serologic studies for toxoplasmosis were performed and resulted in the diagnosis of congenital toxoplasmosis. In spite of therapeutic measures the general condition of the child progressively became worse and he expired on May 8, 1963. A postmortem examination revealed a calcified thrombus in the inferior vena cava.

CASE II. A $4\frac{1}{2}$ year old healthy male was admitted to The Children's Hospital of Philadelphia for evaluation of a bullet-shaped calcification in the right upper abdomen recognized on a survey roentgenogram taken for possible ingestion of a foreign body. The child was perfectly healthy and had normal growth and development since birth. He had been suspected of swallowing a pin by his local physician and roentgenograms of the abdomen obtained at that time revealed no foreign body. A bullet-shaped calcification adjacent to the vertebral column on the right side just below the diaphragm was detected (Fig. 2*A*). Inferior venacavagraphy demonstrated a partially occluded inferior vena cava at the level of the calcification (Fig. 2, *B* and *C*). Since the child was entirely asymptomatic, he was released without further treatment.

CASE III. A full-term baby girl born at the Lankenau Hospital had hydrocephalus. On the third day after birth a ventriculojugular shunt was performed. Her initial hemoglobin was 14 gm. per cent and hematocrit 41 per cent. Four days after the ventricular operative procedure

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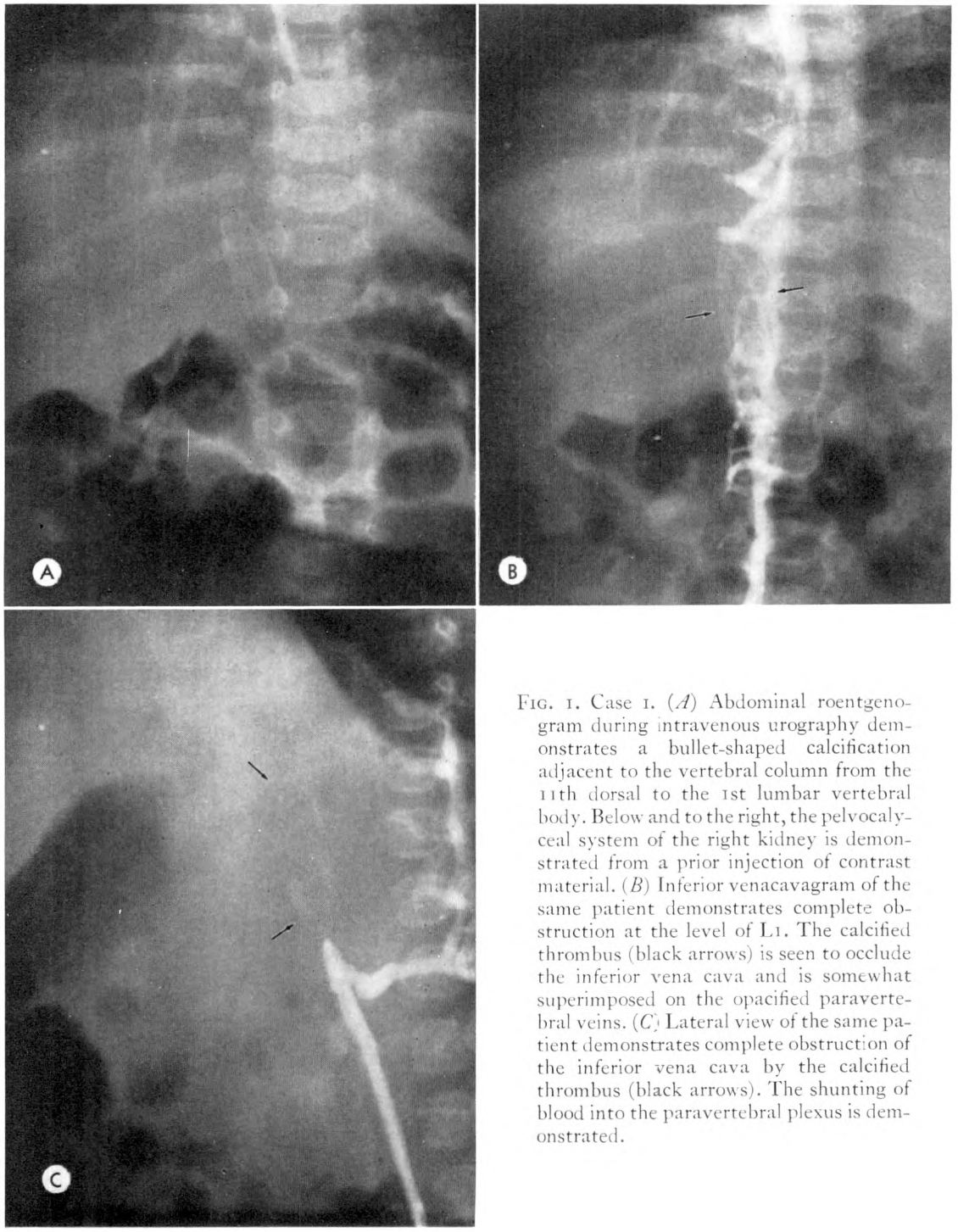


Fig. 1. Case 1. (*A*) Abdominal roentgenogram during intravenous urography demonstrates a bullet-shaped calcification adjacent to the vertebral column from the 11th dorsal to the 1st lumbar vertebral body. Below and to the right, the pelvocalyceal system of the right kidney is demonstrated from a prior injection of contrast material. (*B*) Inferior venacavagram of the same patient demonstrates complete obstruction at the level of L1. The calcified thrombus (black arrows) is seen to occlude the inferior vena cava and is somewhat superimposed on the opacified paravertebral veins. (*C*) Lateral view of the same patient demonstrates complete obstruction of the inferior vena cava by the calcified thrombus (black arrows). The shunting of blood into the paravertebral plexus is demonstrated.

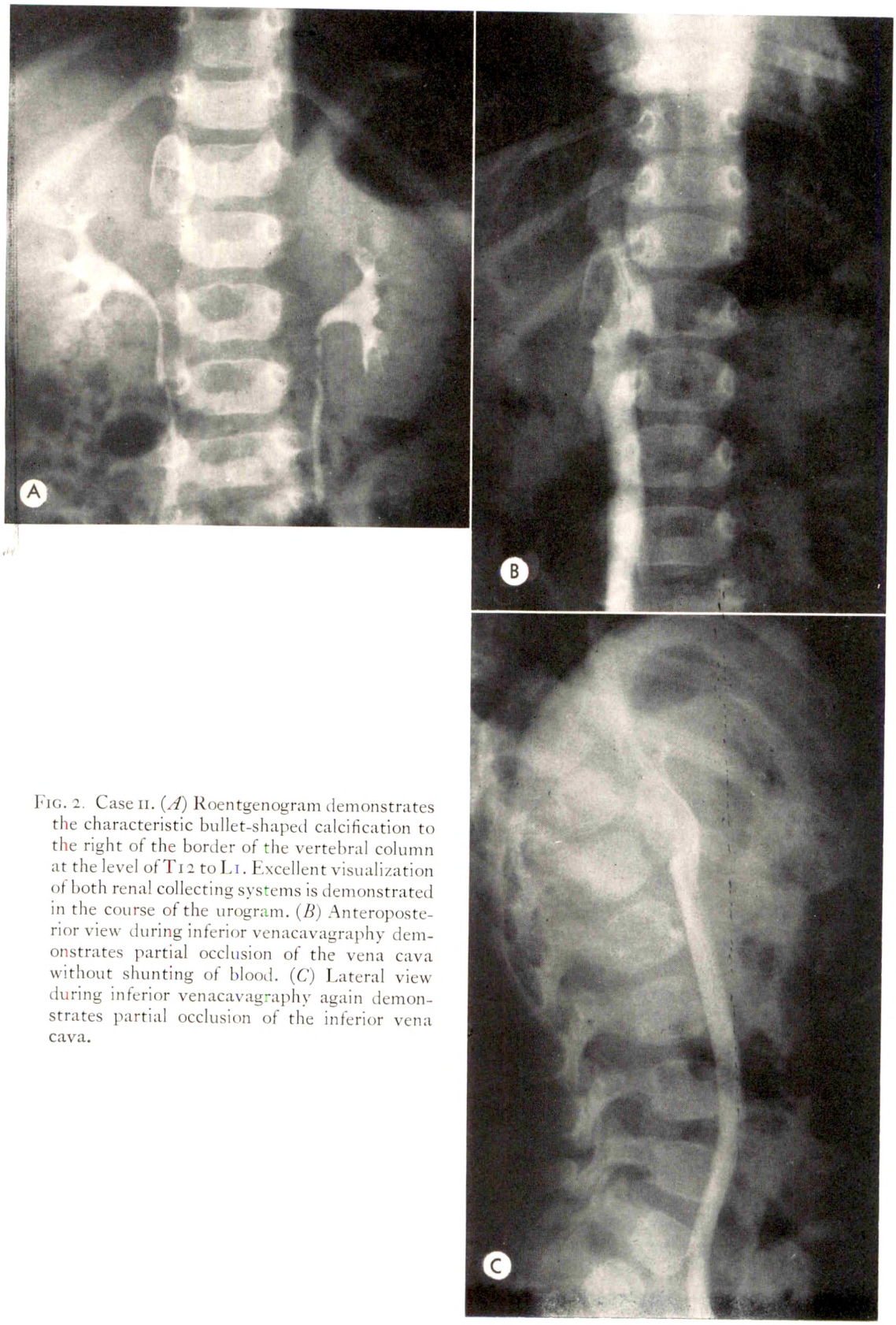


Fig. 2. Case II. (*A*) Roentgenogram demonstrates the characteristic bullet-shaped calcification to the right of the border of the vertebral column at the level of T12 to L1. Excellent visualization of both renal collecting systems is demonstrated in the course of the urogram. (*B*) Anteroposterior view during inferior venacavagraphy demonstrates partial occlusion of the vena cava without shunting of blood. (*C*) Lateral view during inferior venacavagraphy again demonstrates partial occlusion of the inferior vena cava.

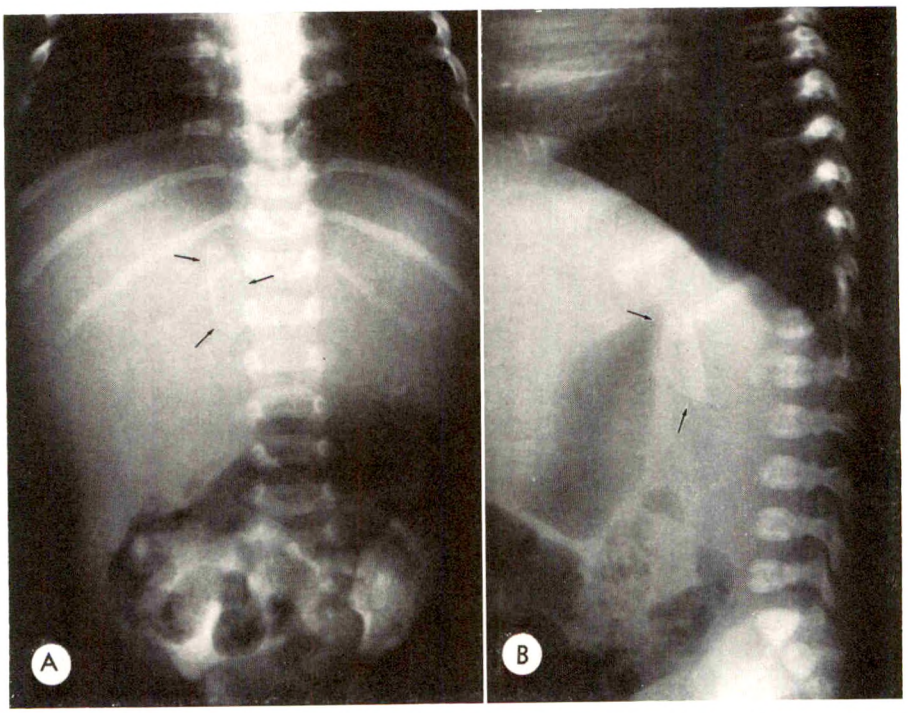


FIG. 3. Case III. (*A* and *B*) Anteroposterior and lateral roentgenograms of the abdomen demonstrate the characteristic bullet-shaped calcification (black arrows) overlying the right 12th rib. Massive hepatic and splenic enlargement is demonstrated. Attempts at inferior venacavagraphy were unsuccessful.

the infant became quite irritable and developed considerable temperature elevation. At this time the hemoglobin had dropped to 7 gm. per cent and the hematocrit to 20 per cent. White blood cell count was 27,200 and platelets were slightly decreased. She was started on penicillin and calcium gluconate. One hundred cubic centimeters of whole blood was also given. On the 11th postnatal day the abdomen became distended. A roentgenogram of the abdomen revealed an enlarged liver and spleen. A bullet-shaped calcification noted just to the right of the spine at the level of the 11th and 12th ribs was thought to indicate a thrombus in the inferior vena cava (Fig. 3, *A* and *B*).

Over the next 3 days the infant became progressively more jaundiced and the bilirubin continued to rise. She expired on the 14th postpartum day. The autopsy revealed subdural and subarachnoid hemorrhage. The bullet-shaped calcification was in a thrombus in the inferior vena cava (Fig. 3, *C* and *D*).

CASE IV. A 12 year old mentally retarded child was admitted to The Children's Hospital of Philadelphia for evaluation following an episode at her home institution, during which the patient had become quite disturbed and had bitten another patient. An extremely limited roentgen examination included survey roentgenograms of the abdomen. This revealed the characteristic bullet-shaped calcification adjacent to the vertebral column just below the right hemidiaphragm. Due to the patient's mental status and freedom from other medical problems, no further studies were attempted. With the previous experiences, this was thought to represent a classical calcification in a thrombosis of the inferior vena cava.

DISCUSSION

In 1896, Unruh described a thrombus in the inferior vena cava associated with a probable endothelial tumor in the same area.[8] This is thought to be the first description of a typical clinical entity. Thrombosis of the inferior vena cava frequently may present with dramatic symptoms of abdominal discomfort, splenomegaly, lower extremity edema, prominent veins and a rapid downhill course to death. In a few instances, reports of slow

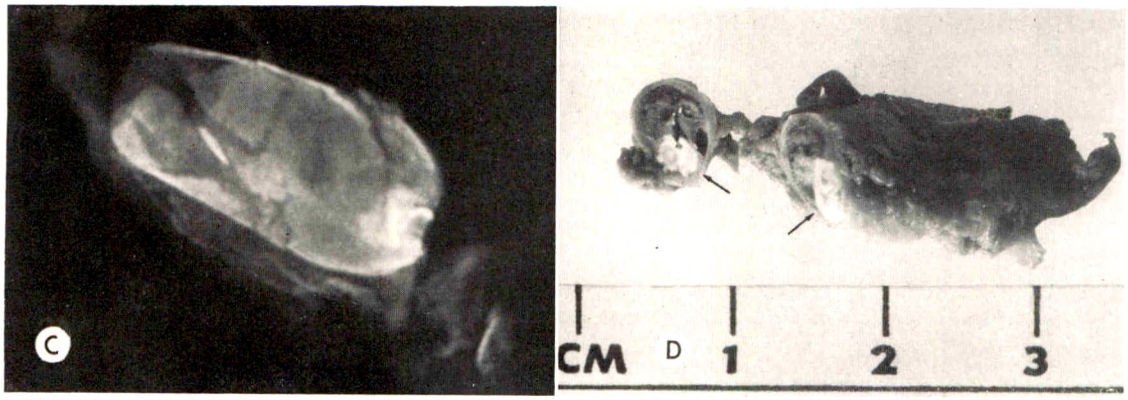


Fig. 3. (*C*) Roentgenogram of the autopsy specimen demonstrates the calcified thrombus within the soft tissues of the vena cava. (*D*) A cross-section of the inferior vena cava demonstrates the densely calcified thrombus adherent to the wall of the inferior vena cava (black arrows). The remainder of the inferior vena cava is occluded with clot which is not calcified.

progression of abdominal distention, edema and hepatic and splenic enlargement, also ending in death, have been described.[1,4] Other than the single report by Singleton and Rosenberg,[7] no other authors have noted the characteristic calcification in the inferior vena cava. The etiology of vena cava thrombosis has been extensively reviewed and 3 general categories described:

1. Generalized or focal infection.
2. Tumors in the region of the liver and vena cava.
3. Anomalies of the inferior vena cava.

The use of inferior venacavagraphy has been well described previously and consists of the rapid injection of contrast media in a leg or femoral vein; at the conclusion of the injection several abdominal roentgenograms are obtained over a 4 to 6 second interval. Characteristic defects in the contrast filled vena cava, as well as collateral venous channels, will be demonstrated in the presence of such a thrombus.

It is apparent that in the acute clinical syndrome, the diagnosis of thrombosis of the inferior vena cava is usually no problem. Knowledge of the rather specific calcification associated with this entity can be useful in the differential diagnosis of abdominal calcifications in the otherwise asymptomatic patient. Since calcifications in the abdomen of children are frequently associated with malignant disease, one should be aware of this presently described roentgenographic entity. Confirmation can be made by inferior venacavagraphy.

SUMMARY

Four cases of children with calcified thrombi of the inferior vena cava are reported. Two children were asymptomatic with respect to this process and 2 of the children died from related diseases.

The characteristic bullet-shaped calcification adjacent to the vertebral column in the right upper abdomen, which was originally described by Singleton and Rosenberg in 1961,[7] was demonstrated in each case and the diagnosis in 2 cases was confirmed by inferior venacavagraphy. Two cases were confirmed at postmortem examination.

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STAPHYLOCOCCAL PNEUMONIA AND EMPYEMA IN CHILDHOOD*

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STAPHYLOCOCCAL pneumonia (apart from its association with fibrocystic disease) is an important disease in infancy and childhood due to the severe morbidity and occasional mortality it causes. Although the subject has been reviewed from the clinical, bacteriologic and epidemiologic aspects, relatively little detailed consideration has been given to the roentgenologic features. A series of 12 cases of staphylococcal pneumonia and empyema are reported to illustrate the major roentgenologic features of the disease.

GENERAL CONSIDERATIONS

In general there has been a decrease in the incidence of childhood pneumonia requiring hospital admission in the last 30 years, but this decrease has not been evident in children under 2 years of age[10] and it is this age group that is particularly affected by staphylococcal pneumonia. This particular infection, however, probably accounts for less than 1 per cent of all childhood pneumonias.[5] It is also of interest that empyema reached its lowest incidence in about 1952 to 1953, but has increased since due to a rising number of cases of staphylococcal empyema. Pneumococcal empyema is now very rare.[6,10]

Staphylococcal pneumonia usually presents in infancy, and in the present series all but 1 of the cases were under 1 year of age. The onset may be explosive, but may present with a few days of nonspecific illness often starting as an upper respiratory tract infection with rapidly increasing severity of respiratory symptoms so that in most cases the child becomes critically ill and requires nursing in an oxygen tent. The disease progresses to its maximum severity in a few days, often reaching this stage by the time the child is admitted. The severity of the toxicity may be clinically manifested by episodes of apnea and the onset of cardiac failure. In spite of the severity of the illness, however, long-term follow-up has not shown any disproportionate number of cases to be particularly liable to chronic or recurrent chest infections. Cases on whom follow-up lung function studies and development records have been kept show no functional impairment or retardation of development compared with their peers.[11]

The bacteriologic diagnosis of staphylococcal pneumonia cannot be made merely on the positive result of a nasal swab in a patient with pneumonia, owing to the possible previous administration of antibiotics producing false negative cultures, while the common nasal carrier state for this organism could produce false positives. Valid sources of the organism are the blood, sputum (not often produced by children), empyema (when it occurs), or autopsy material. Lung puncture has also been advocated.[2] None of these sources of the organism seem to give more than 50 to 60 per cent recovery. Therefore, purely roentgenologic features have to be considered to indicate the diagnosis and may be essential in the period before bacteriologic results are available.

DIAGNOSTIC CRITERIA

In the present series the diagnoses have been based on the following criteria:

(i) Isolation of the organism from empyema or sputum.
(ii) Pneumonia in which characteristic radiolucent areas are observed,[4] usually with supporting evidence in the form of positive culture from nose, throat or rectal swabs.
(iii) Evidence of staphylococcal infection elsewhere than the chest in addition

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to the presence of a severe pneumonia.

MATERIAL

The case material consists of 12 cases all of which satisfy the diagnostic criteria. The ages range from 9 days to 3 years; 10 were under 6 months of age, 1 was 7 months and 1 was 3 years old.

ROENTGENOLOGIC FEATURES

Roentgenologically, the cases can be divided into 2 groups of 6. In the first group of 6 cases, the disease was almost entirely restricted to the lung parenchyma, while in the second group of 6, pleural disease, *i.e.*, empyema or pyopneumothorax, dominated the roentgenologic picture.

Group I. With respect to the pneumonic form of disease, the main roentgenologic feature was the pneumonic consolidation. This may be extensive throughout the lung field, or rather more commonly (4 out of the 6 cases), merely lobar in extent. Bilateral disease did not occur. The density of the consolidation may be such that only in a penetrated roentgenogram will lung markings be seen extending to the periphery and thus excluding the possibility of a large empyema (Fig. 1). Significant pulmonary collapse occurred in only 1 instance (Fig. 2) and in no case did lesions "flit" from one region to another. In all cases there was extensive shadowing in the lung fields when the child was first roentgenographed because of his respiratory symptoms.

In 4 of the 6 cases of this group, air spaces (pneumatoceles) were seen during the illness. In 2 they were evident on the first roentgenogram made and in 2 they appeared later. A fluid level was observed in a pneumatocele on one occasion (Fig. 3). Usually the pneumatoceles disappeared rapidly, but in 2 cases resolution was delayed for 4 weeks and 4 months, respectively (Fig. 4). They appeared to be related to the resolving and re-aeration phase of the pneumonia.

Pleural involvement was conspicuously minimal but was noted in 2 cases in this group, 1 showing a thickened cap of apical pleura at the time of discharge and in the other a shallow pneumothorax with an effusion was present at the height of the predominantly pneumonic illness.

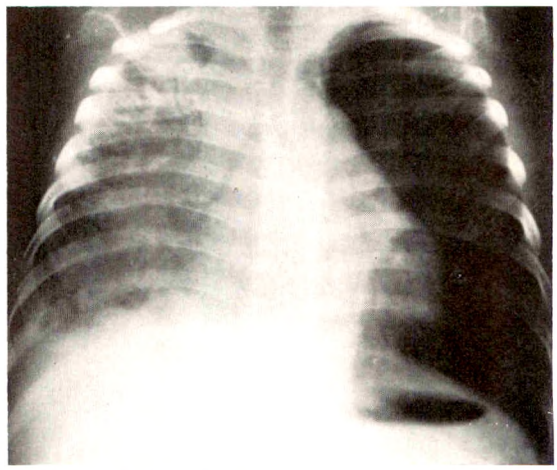


FIG. 1. Penetrated roentgenogram showing extensive pneumonia in the right lung. The routine roentgenogram showed an almost totally opaque right hemithorax.

One case in this group warrants particular mention as the pneumonia followed a staphylococcal infection of the skin.

CASE 1. This was a 9 day old child on whom a laparotomy was performed for relief of intestinal obstruction due to inspissated milk curds. On the third postoperative day wound infection was noted and culture of the exudate showed profuse growth of *Staphylococcus aureus*. Ampliclox apparently controlled the infection for a

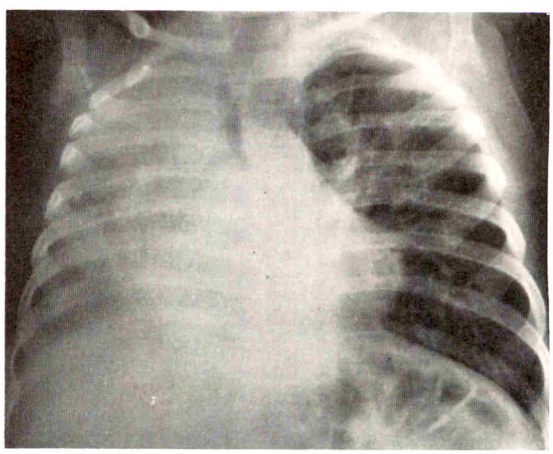


FIG. 2. Collapse of the right upper lobe with shift of the superior mediastinum and herniation of the left upper lobe.

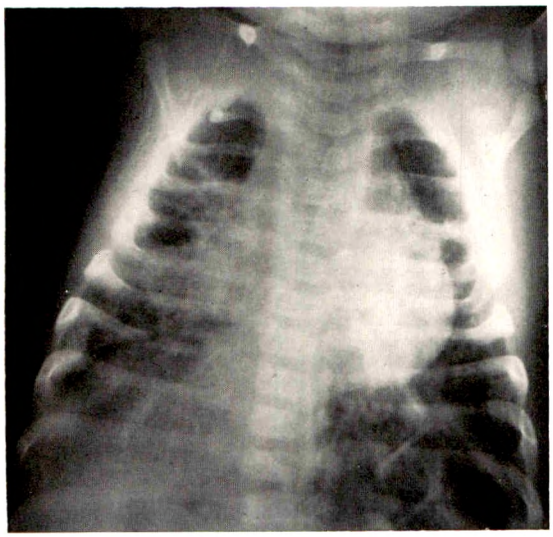


Fig. 3. Right lower lobe pneumonia with pneumatocele formation. A fluid level is shown in one pneumatocele.

period but the respiratory rate and temperature started rising again on the 14th postoperative day. The chest roentgenogram (Fig. 5) showed extensive consolidation of the right middle and lower lobes producing an almost opaque hemithorax through which a number of clumped translucencies could be seen. On the basis of a known staphylococcal wound infection and the roentgenologic appearances, a diagnosis of staphylococcal pneumonia with pneumatocele formation was made.

Group II. The second group of 6 cases

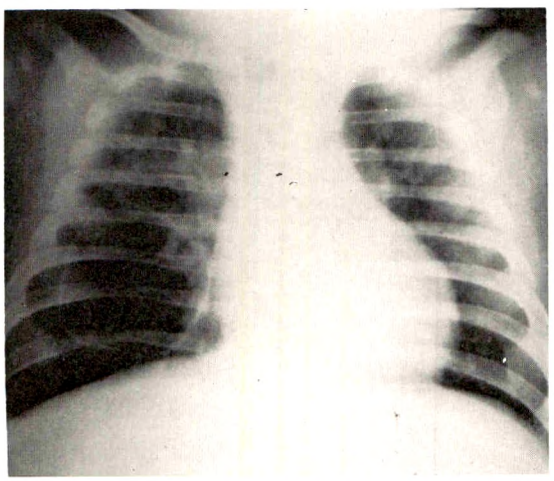


Fig. 4. A large pneumatocele in the right lower lobe which persisted for 4 months after resolution of the pneumonia.

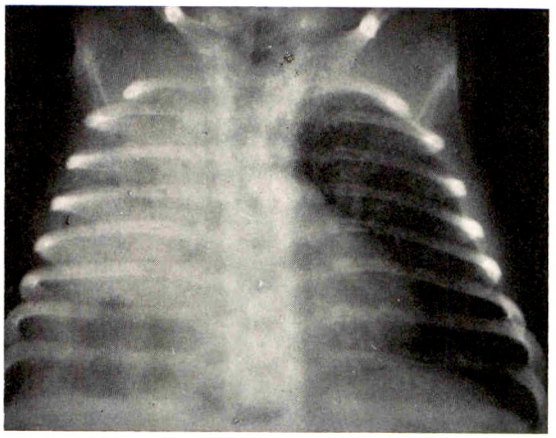


Fig. 5. Extensive consolidation in the right lung showing clumped pneumatoceles at the base and peripherally in the mid-zone.

was dominated roentgenologically by extensive and severe pleural disease; these 6 cases can again be subdivided into 3 cases with empyema alone and 3 with pneumothorax or pyopneumothorax. Of the first 3 cases, the roentgenologic presentation was empyema in 2; 1 showed pneumonic consolidation, the empyema developing subsequently. Of the 3 cases progressing to pyopneumothorax, the presentation was pneumonia, empyema and pneumothorax in each of the 3. Usually the advent of an empyema or a pyopneumothorax is marked by worsening of the clinical condition. Roentgenologically the empyemas were extensive and produced total opacity of one lung field through which, however, the air spaces of pneumatoceles could sometimes be distinguished (Fig. 6). Likewise the pyopneumothoraces demonstrated extensive pleural involvement by the large fluid level which extended across the affected side of the chest (Fig. 7), or the size of the pneumothorax. If a supine roentgenogram is taken, the characteristic horizontal fluid level is absent and there may be confusion with a large tension cyst (Fig. 8). However, in all cases of pleural involvement (empyema or pyopneumothorax) there was extensive and marked pleural thickening during resolution (Fig. 9). The only fatal case was one with empyema, the autopsy showing lung abscesses and a bronchopleural fistula.

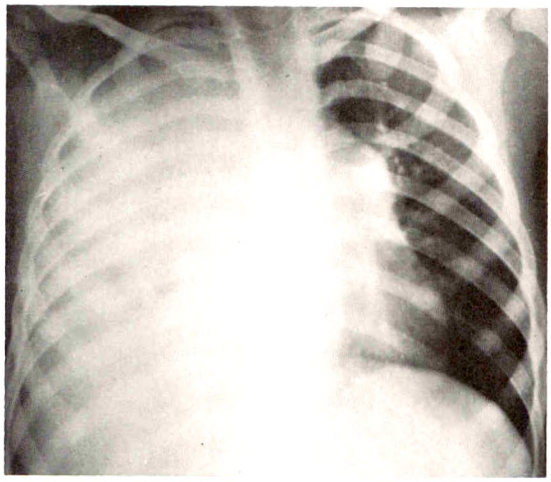


FIG. 6. Right-sided empyema. The translucencies of pneumatoceles in the lower zone can be seen through the overlying opacity.

The cases of pleural involvement tended to have a more severe clinical course than those restricted to the lung parenchyma. Among the 6 cases of empyema or pyopneumothorax, 3 were noted to have congestive cardiac failure and 1 of these had episodes of apnea. On the other hand, of the purely pneumonic cases, only 1 had apneic episodes and none manifested cardiac failure.

The particular association of staphylococcal infection elsewhere than the chest

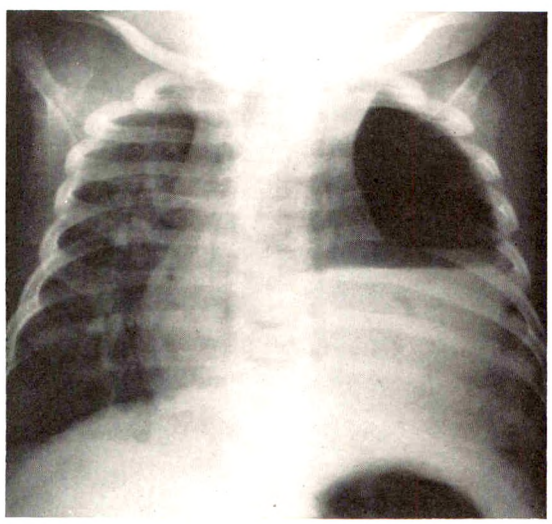


FIG. 7. Left-sided pyopneumothorax showing the typical long fluid level and some mediastinal shift to the right.

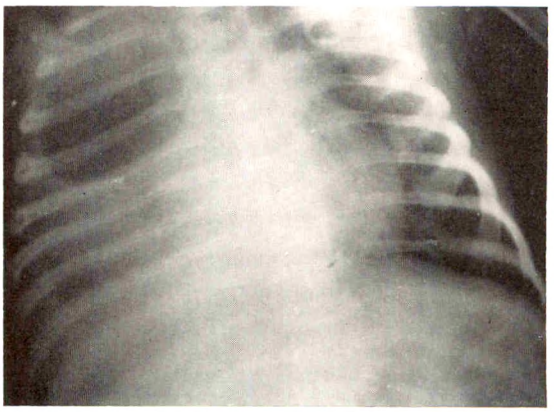


FIG. 8. A pyopneumothorax demonstrated on a supine roentgenogram. The typical fluid level is absent.

among the cases with pleural involvement should be noted; thus, there were 2 cases of purulent otitis media from which a *Staphylococcus aureus* was grown and there was 1 case with rather doubtful otitis media. Yet another case with extensive staphylococcal infection may be noted in more detail.

CASE II. A female child, aged 5 months, had been admitted elsewhere with a diagnosis of bronchopneumonia. Treatment with antibiotics had been given, at the end of which time intractable diarrhea and vomiting began, for which she was transferred to the Paediatric Unit of St. Mary's Hospital.

On admission the child was markedly dehy-

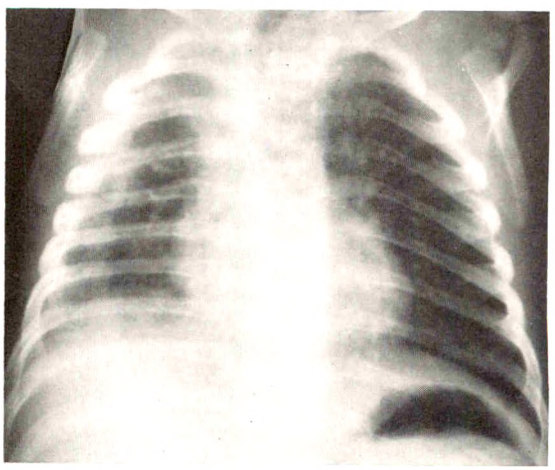


FIG. 9. Same case as in Figure 8. This roentgenogram shows the peripheral pleural thickening typical of resolving empyema, proving the nature of the translucency in the previous roentgenogram.

drated, mild skin sepsis was noted on the left buttock and around "cut down" areas on the right leg. The lung fields appeared clear. Subsequent skin abscesses on the left hand and leg appeared for which penicillin and fucidic acid were given. Pus from these grew *Staphylococcus aureus*. Two weeks later there was clinical and roentgenologic evidence of osteomyelitis of the third metacarpal. Following this discovery the child became more febrile and tachypneic. A chest roentgenogram showed a tension pneumothorax with mediastinal shift and lung herniation. A small quantity of basal fluid and extensive thickening of the parietal and visceral pleural surfaces were also shown (Fig. 10). The antibiotic regime was continued; serial roentgenograms revealed resolution of the pneumothorax and of the pleural thickening prior to complete reversion to normal.

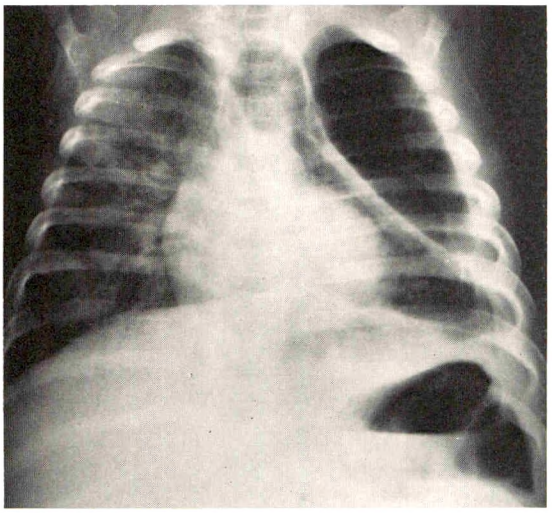


Fig. 10. Left-sided pneumothorax showing mediastinal shift and lung herniation. The visceral and parietal pleural surfaces are thickened. There is only a small quantity of pus in the lower part of the pleural cavity.

DISCUSSION

The major clinical features of staphylococcal pneumonia having already been described, the discussion will be restricted to the roentgenologic manifestations of the disease.

PNEUMONIC CONSOLIDATION

A region of consolidation may be the presenting roentgenologic sign, particularly if the roentgenogram is taken at a suitably early stage of the disease. The consolidation may be relatively restricted or extensive and occasionally is the sole roentgenologic feature throughout the course of the disease. More often, pneumatoceles are seen in the region of consolidation.

PNEUMATOCELE FORMATION

Pneumatoceles are thin-walled cystic spaces appearing within the region of consolidation and are the most widely recognized features of staphylococcal pneumonia; although a common manifestation, they are not invariably present. They may vary considerably in size and number and can sometimes be seen in the affected lung through the opacity of an overlying empyema. Their natural history is towards regression, which, however, may be delayed for weeks or even months. This tendency to regression of pulmonary cysts in childhood, most of which are postinflammatory and not congenital, was noted by Caffey,[1] who therefore advised against surgery except in the very occasional case in which the pneumatocele continued to enlarge and cause respiratory distress, when excision may be necessary.[9]

The mechanism of formation is believed to be a valve-like action developing due to obstruction of the terminal bronchi resulting in distal air trapping.

Although the development of pneumatoceles is a characteristic feature of staphylococcal pneumonia, they have also been observed in treated miliary tuberculosis in children,[3] kerosene (paraffin) inhalation pneumonia,[8] pneumococcal and streptococcal pneumonia.[10]

ABSCESS

Thick-walled abscess cavities are not common in childhood staphylococcal pneumonia, but were found at autopsy in the single fatal case. When they occur they tend to be multiple, clumped and vary in size.[7]

EMPYEMA

Empyema is a common manifestation of staphylococcal pneumonia and a large empyema occurred in 5 cases in our series. It

often dominates the roentgenologic picture and may obscure the underlying lung lesion, although the translucency of pneumatoceles may occasionally be seen through the opacity. The empyema is frequently present by the time a patient is admitted to hospital and is usually large enough to produce a totally opaque hemithorax with mediastinal shift to the opposite side. The extensive opacity of an empyema may be difficult to distinguish from a similar appearing opacity due to extensive pulmonary consolidation. A more penetrated roentgenogram will demonstrate the pleural thickening of the empyema, whereas in extensive consolidation the lung markings may be seen within the opaque area extending to the periphery. During resolution of the empyema it characteristically leaves a margin of thickened pleura which may be visible for months before it completely resolves.

PNEUMOTHORAX

This usually occurs in association with empyema forming a pyopneumothorax, when a long air fluid level is seen on the affected side of the chest extending to the peripheral pleural surface. In 1 case the quantity of fluid was small but the extensive pleural thickening was well shown on both aspects of the large pneumothorax space. The pneumothorax probably forms as a result of rupture of subpleural pneumatocele or abscess,[6] although such a postulated lesion may not be roentgenologically demonstrable. The onset of the pneumothorax may be dramatic or insidious and often portends a bronchopleural fistula when there is free escape of air into the underwater drain. During resolution the pleura shows thickening as in empyema.

Differentiation of pyopneumothorax from a large pneumatocele may be difficult, especially if a supine roentgenogram had to be taken when the characteristic fluid level will be absent. In retrospect, the diagnosis may be clarified when the pleural thickening characteristic of resolving pyopneumothorax becomes evident.

SUMMARY

Twelve cases of staphylococcal pneumonia and empyema are reported. Roentgenologically, they consisted of 6 cases of pneumonic consolidation with or without pneumatocele formation and with little evidence of pleural disease, and 6 cases with severe pleural disease, empyema or pneumothorax.

Attention is particularly drawn to the fact that 3 of the cases of empyema and 1 of pneumonia had good evidence of associated staphylococcal infection elsewhere; *i.e.*, in the skin, bone or middle ear.

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FISSURE LINES IN THE PEDIATRIC ROENTGENOGRAM*

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A LARGE portion of inflammatory diseases in children is centered or reflected in the chest. It is important to recognize minute changes that would lead the physician to early diagnosis.

The visceral pleura many times gives evidence of disease in its early stages; however, there is no study of what the visceral pleura is expected to look like in the normal child's chest. We have undertaken to evaluate the interlobar portions of the visceral pleura in order to establish a norm that can be used to evaluate changes that might occur in abnormal states and compare the normal with specific disease processes.

The normal visceral pleura is very thin with only a few cell layers[10] present. It is closely attached to the pulmonary parenchyma and cannot be separated easily. Each lobe of the lung is either partially or completely enveloped with the visceral pleura (excluding the lung root). The interlobar fissures are areas where the visceral pleura can be visualized on roentgenograms[4,5,7,8] due to the double thickness of the investing pleura of adjacent lobes and the contrasting air on either side of the fissure line. Even this doubling effect is not enough to roentgenographically visualize the interlobar fissures unless fairly large planes of the fissures are parallel with the roentgen-ray beam.[9]

The position of the minor or transverse interlobar fissure is most nearly in a horizontal plane both in the posteroanterior and lateral views of the chest. It is thus more easily seen. The longitudinal fissures are best seen in the lateral views because in this position they are most nearly on edge to the roentgen-ray beam. It is very unusual to see the longitudinal fissures in the posteroanterior view and when seen it is only in the lower third of the chest.[3,11]

It is also reasonable to expect considerable variation in visualization of the fissures due to variation in shape of the lobes. If the interface between the lobes is relatively flat, long fissure lines can be seen when the plane is nearly parallel with the roentgen-ray beam. If the interlobar interfaces are considerably curved, the amount of fissures on edge to the viewer is very small and the likelihood of seeing a fissure line is very small.

Consecutive pediatric chest roentgenograms were examined at Southern Baptist Hospital and Charity Hospitals by the authors. The clinical history was recorded in each case to determine the presence or absence of any known chest disease. If either the clinician or radiologist suspected chest disease the case was considered abnormal. Only those cases in which both the clinical and roentgenographic examinations were normal were used as normal cases.

Each case had both an erect posteroanterior and lateral view. The roentgenograms were included only if the position was true and the degree of inspiration was adequate.

The volume of the chest was obtained by 4 simple measurements (Fig. 1). This method gives a rough but relatively constant volumetric measure that is within 10 per cent of the expected volume obtained by the more accurate method of Loyd and his co-workers.[6]

The 2 views of the chest of each case

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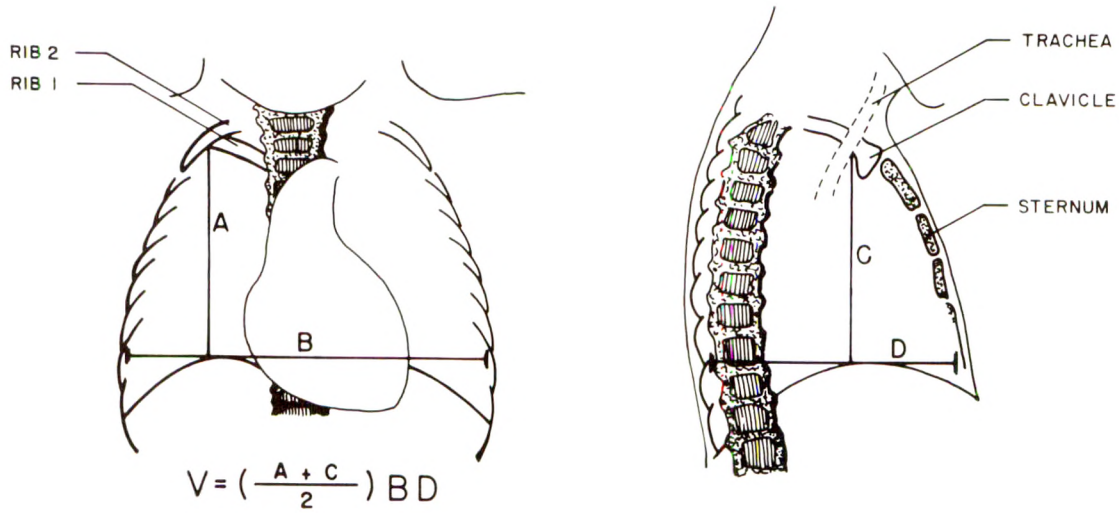


FIG. 1. Measurement of thoracic volume. Line A is the distance from the right diaphragm to the point where the anterior first rib crosses the posterior second rib at approximately the mid-clavicular line. Line B is the transverse diameter of the lower chest at the average level of the 2 diaphragms. Line C is the height of the chest in the lateral view from the point where the anterior portion of the clavicle crosses the trachea to the average height of the diaphragms. Line D is the anteroposterior diameter of the chest at the average height of the diaphragms. Thoracic volume, $V=[(A+C)/2]BD$.

were then examined for presence or absence of fissure lines. These were recorded and tabulated (Fig. 2). Additional information concerning the degree of inspiration, relative height of the diaphragms, and hilar areas was recorded.

RESULTS

One hundred and eighty-six cases were considered normal. These ranged in age from the newborn to over 12 years. One hundred and nineteen examinations demonstrated fissure lines in 1 of the 2 views but usually in the lateral view.[4] Thus 64 per cent of normal chests in children qualitatively demonstrated fissure lines (Fig. 2, Line N). The percentage showing fissures demonstrated a steady increase with age with the exception of the first few weeks of life when the number dropped rapidly. This should be expected due to the large amount of fluid in the newborn infant's body and the rapid loss of this excess fluid during the first few weeks of life. The line N approaches 100 per cent for adults.

For comparison we have evaluated over 700 consecutive adult chest roentgenograms and have yet to find one in which fissure lines could not be seen.

Four hundred and eighty-three children were considered abnormal. Of these, 365 demonstrated fissure lines indicating that

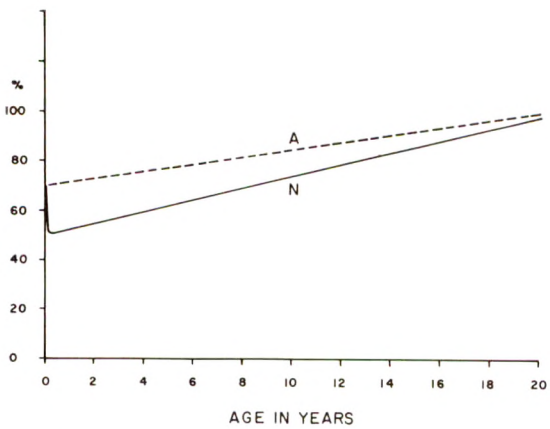


FIG. 2. Fissure lines in pediatric chests: a qualitative evaluation. This graph indicates the frequency of presence of visible fissure lines in 673 pediatric chest roentgenograms—190 normal and 483 abnormal. The solid line (N) represents the percentage of normal chests that demonstrated fissure lines by age, and the dashed line (A) represents the abnormal chests.

75 per cent of abnormal pediatric chest roentgenograms will show fissure lines (Fig. 2, Line A). The variation is from 70 per cent at birth to 100 per cent in adulthood. It is interesting to note that in this abnormal group we were unable to detect the expected decrease in percentage in the first few days after birth as in the normal group. This would indicate that abnormal acute states would tend to accentuate the fissure lines as expected. This accentuation is present throughout the various age periods as indicated by the space between the abnormal and normal groups in Figure 2.

Quantitative evaluation was made on the total length of visible fissures in a sample group including 81 normals, 72 post-tuberculosis patients and 50 children with cystic fibrosis (Fig. 3). The graph presents a composite of the expected average curves as indicated by the sample groups and is determined by using the centimeters of total visible fissures in 2 chest views as the ordinate and the thoracic volume as the abscissa.

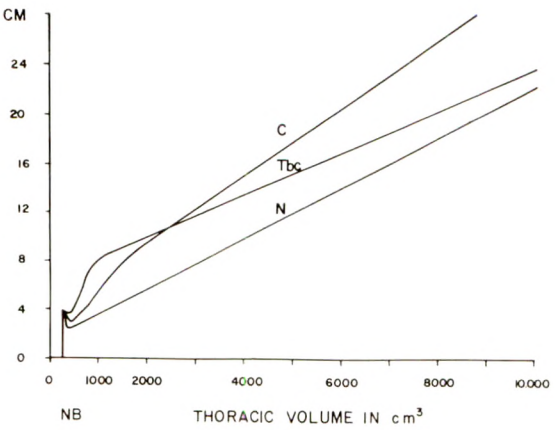


Fig. 3. Pediatric chest fissure lines: quantitative evaluation. This is a composite of the visible fissure lines. The ordinate is in cm. of fissure length and the abscissa is the thoracic volume in cm.³. Line N represents the normal group. Line Tbc represents the findings in post-tuberculosis chest roentgenograms. Line C represents the fissure length in children with cystic fibrosis.

DISCUSSION

The presence of visible fissure lines in childrens' chest roentgenograms is a normal finding.[1] The contention that these fissure lines are abnormal beyond the first few weeks[2] is erroneous. We have found that approximately 70 per cent of normal newborn chest roentgenograms will demonstrate fissure lines. This percentage decreases rapidly to about 50 per cent at 1 month and then progressively increases with age reaching 70 per cent again at about 9 years of age and 100 per cent somewhere beyond 20 years (Fig. 2). It is rare not to see fissure lines in adults.

In the abnormal chest the percentage of children having fissure lines is increased over the normal. At birth 70 per cent show these lines. There is then a steady increase in the percentage with fissures reaching the 100 per cent mark somewhere beyond 20 years. The early decrease in the visualized fissures as seen in the normal chest does not occur in the abnormal group, indicating that acute inflammatory diseases of the chest causes accentuation of the fissures either by fluid in the pleural space or by fluid collection in the lung adjacent to the pleura. When the acute phase is over, the accentuation disappears and the per cent visualization returns to the expected normal line. This return to normal, however, does not occur in patients with tuberculosis or cystic fibrosis.

The quantitative evaluation of the fissure lines visualized in the pediatric chest roentgenograms follows a curve similar to that of the qualitative evaluation. At birth an average of 3.8 cm. fissure length can be seen. This decreases to approximately 2.4 cm. average within a few weeks and then increases steadily while the size of the thorax is increasing (Fig. 3).

There is a marked difference in the length of the visible fissures in patients who have had tuberculosis. Following the acute stage there is permanent accentuation of the fissures as shown by greater measurable length in each age group and this difference persists up to adulthood. The difference from the normal is most pronounced

up to 10 years of age but is still demonstrable beyond this age.

This finding in post-tuberculosis patients suggests that the tuberculous infections nearly always affect the pleura as well as the pulmonary parenchyma in its acute phases even though we may not recognize these changes. The finding of longer visible fissure lengths on a chest roentgenogram may provide an additional indication that tuberculosis has been present in the past.

Cystic fibrosis is another disease that accentuates the fissure lines in the pediatric chest. In evaluation of 50 cases the chest roentgenogram early demonstrated a deviation from the normal group. The measurable difference exceeds that of post-tuberculosis patients at about 4 years of age and continues to increase at a much greater rate than the normal. This is most likely due to the repeated bouts of inflammatory disease that these children have, but does not exclude the possibility of pleural accentuation due to altered pulmonary and pleural anatomy as a result of the disease process.

A more detailed evaluation of serial chest roentgenograms of the cystic fibrosis patients adds another interesting finding (Fig. 4). Line B represents measurable fissure length at the time the cases were recognized and therapy instituted. Line A is a re-evaluation of the chest roentgenograms of these patients 1 to 4 years after they had been on treatment. The differences are not large but are consistent in all age groups. It is difficult to determine whether this difference is due to the likely presence of acute disease in the first roentgenograms as compared with no acute infection in the later stages, or if this difference represents a decrease in rate of progression of the permanent effects of the disease.

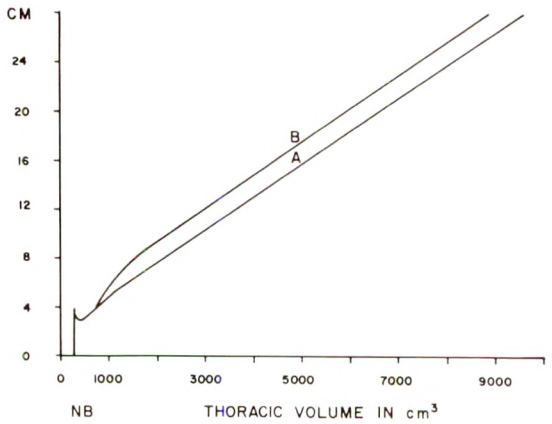


FIG. 4. Fissure lines in pediatric chests in cystic fibrosis. This is a comparison of the same group of patients demonstrating the measurable amount of fissure lines before treatment began (Line B) and after the child had been on treatment (Line A) for 1 to 4 years. The ordinate is in cm. of fissure length and the abscissa is the thoracic volume in $cm.^3$.

SUMMARY

The fissure lines in pediatric chest roentgenograms have been largely ignored. This study evaluates the frequency and length of fissures in the normal chest roentgenogram. They are also equated with the quantitative effect of disease processes such as tuberculosis and cystic fibrosis.

The acute lung diseases show an increase in number and length of visible fissures but return to normal following the acute phase. In tuberculosis and cystic fibrosis the changes are permanent and can be recognized by comparison with the expected norm.

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EMPYEMA IN CHILDHOOD FOLLOWED ROENTGENOGRAPHICALLY: DECORTICATION SELDOM NEEDED*

By PHILLIP L. SMITH, M.D.,† *and* BARRY GERALD, M.D.†‡
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EMPYEMA in childhood is no longer associated with the grave prognosis that existed before the advent of antibiotics.[1] However, the roentgenographic appearance of a persistently opacified hemithorax due to pleural fluid or fibrous exudate is often a cause for concern, even though the patient may be relatively asymptomatic.

The purpose of this paper is to acquaint the radiologist with the course of childhood empyema as modified by current therapy so that he may be better able to predict the eventual outcome of the disease.

MATERIAL AND METHOD

This series includes all cases of empyema occurring in children admitted to the University of Arkansas Medical Center over an 8 year period. Twenty-three cases were collected with an age range of 5 days to 14 years.

The patients were seen with symptoms and physical findings of pneumonia. Several had been treated elsewhere before referral to this hospital. The initial roentgenogram in each showed pneumonia with varying amounts of pleural fluid. A thoracentesis was performed in 21 patients and each yielded purulent fluid, the diagnostic criterion for empyema. The 2 patients in whom a thoracentesis was not performed died shortly after admission. Symptoms and physical findings of pneumonia were present. In addition, an opacified hemithorax was present in both patients roentgenographically. These 2 patients were presumed to have empyema as a complication of pneumonia and are included in the series. They represent the only deaths in our series.

Bacteriologic studies were performed on the pleural fluid obtained in 21 cases. Cultures from 7 patients grew *Staphylococcus aureus*, 5 grew *pneumococci* and 1 grew *Staphylococcus albus*. The fluid from 1 patient was accidentally autoclaved. The remaining 7 patients had no culture diagnosis. Of these 7 patients, 5 had received antibiotics prior to admission.

Roentgenographic findings varied from a moderate amount of fluid to complete opacification of a hemithorax. One patient developed a bronchopleural fistula during the hospital stay (Fig. 1, *A*, *B* and *C*) and a second presented with a pyopneumothorax (Fig. 3, *A* and *B*). Two patients developed pneumatoceles. In both instances, the pneumatoceles occurred as the empyema was resolving and disappeared spontaneously.

Each of the 21 patients in whom a thoracentesis was performed was treated with antibiotics and pleural drainage (Fig. 2, *A* and *B*). In 9 patients, pleural drainage was accomplished by repeated thoracentesis only. Nine patients required closed chest drainage. One of these patients was subsequently converted to open drainage with the removal of many large fibropurulent lumps from a 250–300 cc. cavity at surgery. The remaining 3 patients were treated with open chest drainage after thoracentesis.

In 1 patient, a decortication was performed 9 weeks after the onset of symptoms and 21 days after admission to this hospital. In retrospect, the decortication might have been avoided despite the long duration of the illness.

RESULTS

As previously described, 2 patients expired shortly after admission. The other 21 patients responded to therapy and were

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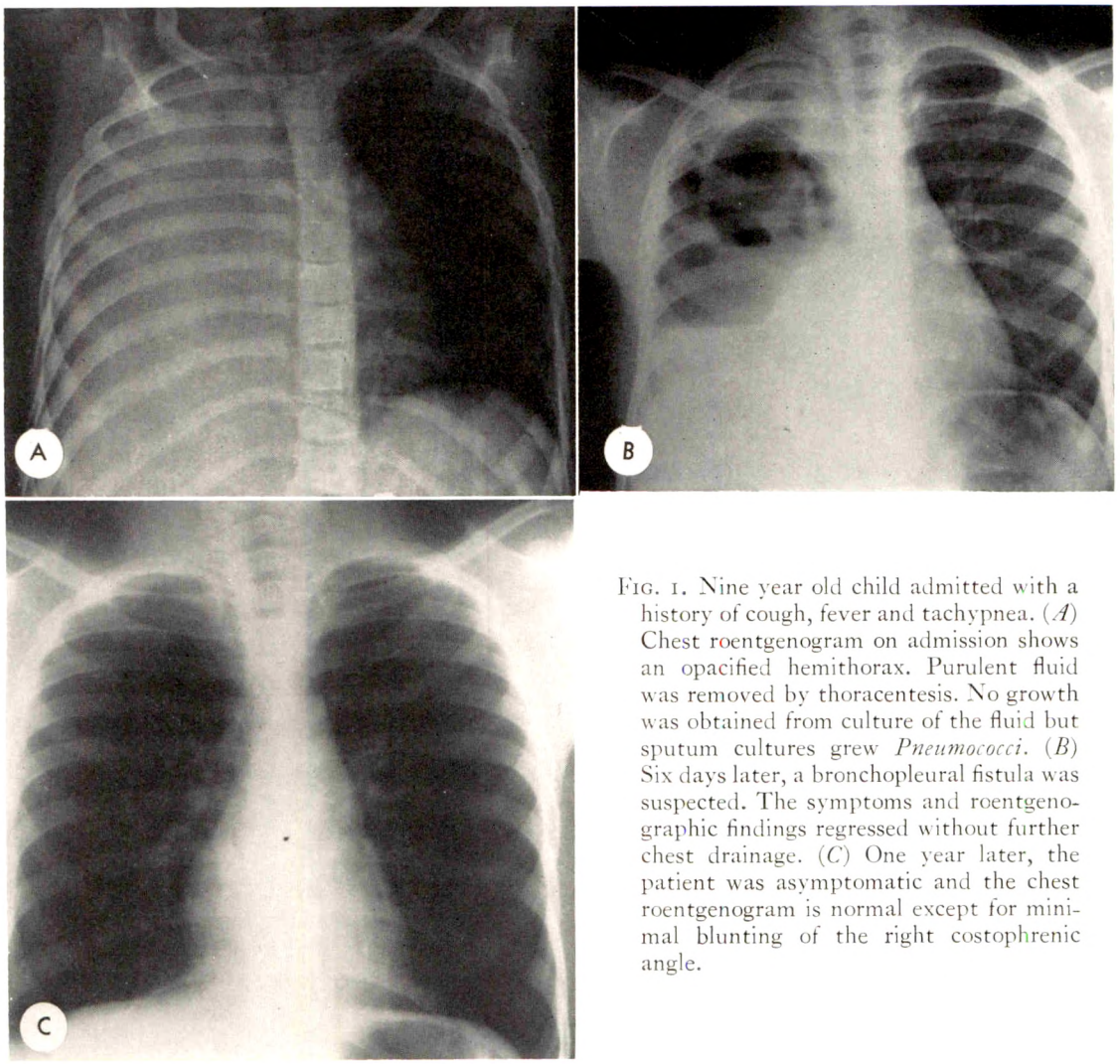


Fig. 1. Nine year old child admitted with a history of cough, fever and tachypnea. (*A*) Chest roentgenogram on admission shows an opacified hemithorax. Purulent fluid was removed by thoracentesis. No growth was obtained from culture of the fluid but sputum cultures grew *Pneumococci*. (*B*) Six days later, a bronchopleural fistula was suspected. The symptoms and roentgenographic findings regressed without further chest drainage. (*C*) One year later, the patient was asymptomatic and the chest roentgenogram is normal except for minimal blunting of the right costophrenic angle.

discharged free of symptoms. The duration of the hospital stay varied from 10 days to 5 weeks.

Four patients were lost to follow-up after discharge; however, each patient was asymptomatic and the roentgenograms in each were normal at the time of discharge. The other 17 patients were followed for 3 months to 4 years. Roentgenographically, minimal widening of the pleural space was noted in some patients but this cleared during the period of observation. In those patients followed over 1 year, the roentgenograms of the chest showed no residual changes from the empyema and the patients remained asymptomatic.

DISCUSSION

Empyema in childhood is usually secondary to pneumonia, with *Staphylococcus aureus* being the most common infecting organism.[5] Antibiotics and chest drainage are the proven means of therapy.[2,4,6]

A needle thoracentesis is usually performed following the diagnosis of empyema and as much of the pleural fluid removed as possible to obtain bacteriologic studies and to restore to normal any cardiopulmonary disability produced by the fluid.[3] The pleural cavity may be drained by repeated needle punctures, closed tube drainage or open tube drainage. Which method is best and the indication for each are controver-

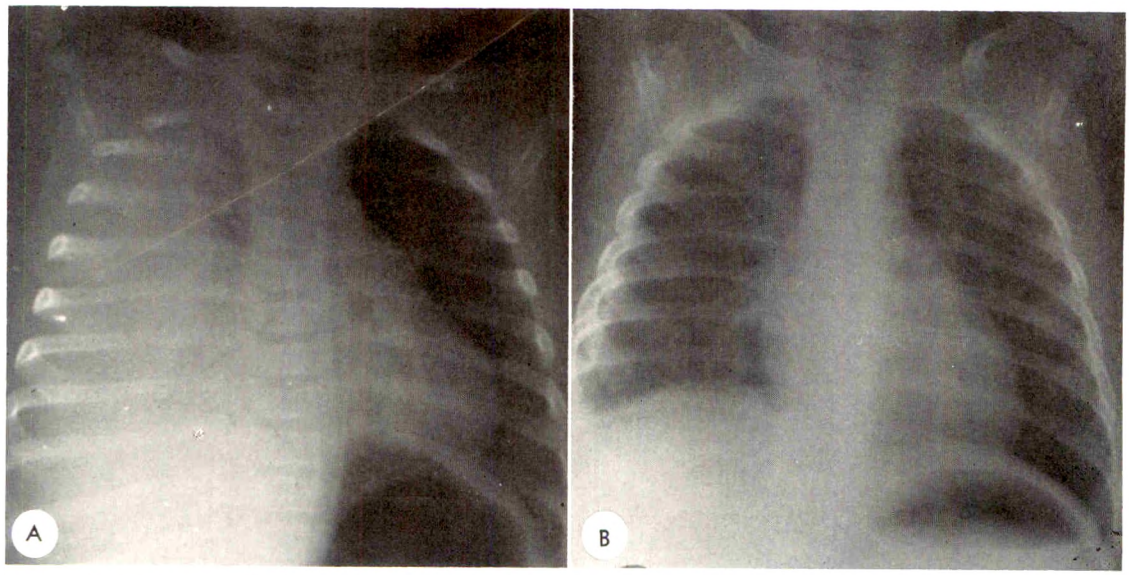


FIG. 2. Three month old child with a history of cough and fever. (*A*) Chest roentgenogram on admission reveals an opacified hemithorax. Seventy cubic centimeters of purulent fluid was removed. Cultures of the fluid grew *Staphylococcus aureus*. Subsequently the child developed a pyopneumothorax and was treated with tube drainage. (*B*) One month later, the pleural space on the right was slightly widened but otherwise the chest was normal roentgenographically and the child was asymptomatic.

sial and further discussion is beyond the scope of this paper.

Broad spectrum antibiotics are given until a specific bacteriologic diagnosis is made. At that time, a drug to which the organism has proved sensitive is begun.

With current methods of therapy, mortality has decreased from a point approaching 100 per cent to some series reporting no fatalities.[1] The 2 patients who died in our

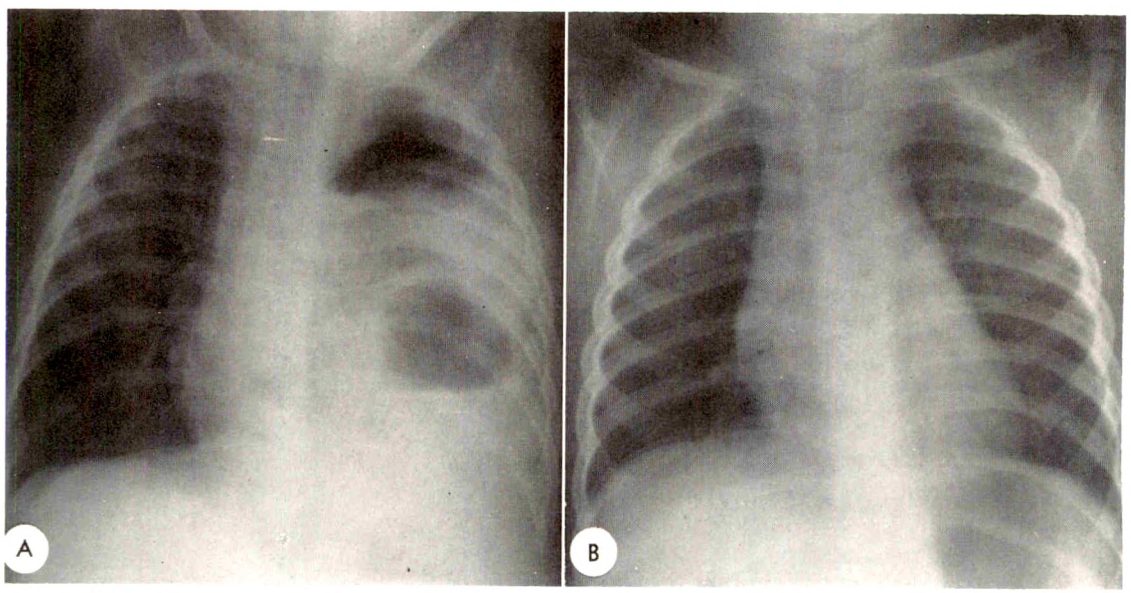


FIG. 3. Nine month old child admitted with 2 week history of cough, respiratory distress and fever. (*A*) Chest roentgenogram on admission shows pneumonia, pleural fluid and a cavity. Cultures of the pleural fluid after thoracentesis and blood cultures grew *Staphylococcus aureus*. A chest tube was inserted and antibiotics begun. (*B*) Four months later, the patient was asymptomatic and the roentgenogram of the chest is normal.

series were moribund on admission and died before therapy could be effective.

A dreaded sequela of empyema in adults is that the thickened pleura may prevent expansion of the ipsilateral lung. The accepted means of therapy for this complication of empyema in adults is decortication with removal of the pleural rind. In contrast to adults, the child is able to resorb the thickened pleura amazingly effectively, perhaps due to the greater elasticity of the lungs and thoracic cage. Rarely is decortication required after empyema in childhood.[3]

Thomas *et al.*[7] have reported the only recent large series of children in whom decortication was performed following empyema. Sixteen patients had decortication performed, but it was not stated how many patients did not require decortication. The average time from onset of symptoms to decortication was 25 days. In our series, as well as in other reports, symptoms, physical findings and roentgenographic manifestations have sometimes been marked at 3 to 4 weeks after onset of symptoms but have cleared completely without resort to decortication.

Wise and co-workers[8] reported a group of patients with *Staphylococcus* pneumonia and empyema in childhood who had been followed 5 to 16 years. Decortication was performed in none of these patients. Each patient was asymptomatic at the time of follow-up with normal pulmonary function studies and normal roentgenograms. In our patients, the final roentgenogram was normal on each patient followed over 1 year. None of our patients exhibited any clinical findings of altered respiratory physiology after discharge from the hospital or on follow-up visits.

The early roentgenographic findings in empyema are striking and may prompt the unwary into decortication, an overly aggressive treatment. It is important that the radiologist be aware of the good prognosis in these patients and guide his surgical and medical colleagues to a practice of watchful waiting. The final criterion determining the role of decortication in empyema of childhood should be the clinical status of the patient rather than the severity of the roentgenographic changes.

SUMMARY

Twenty-three cases of empyema in patients under 16 years of age have been seen at the University of Arkansas Medical Center over an 8 year period. Twenty-one of these patients survived with antibiotic therapy coupled with various methods of chest drainage. Despite marked roentgenographic changes in each patient, decortication was performed only in 1 instance. In the other patients, the roentgenograms showed a return to normal and the children were clinically asymptomatic.

It is important for the radiologist to be aware that the changes seen in empyema of children will almost always regress to normal without resorting to decortication.

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BRONCHOPULMONARY SEQUESTRATION WITH VENOUS DRAINAGE TO THE PORTAL VEIN*

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PULMONARY sequestration is a developmental anomaly of the lung consisting of partial or complete separation of a portion of pulmonary tissue from the rest of the lung.[2] Two types of pulmonary sequestration are recognized, the intralobar and extralobar types.[2,3,6] In the extralobar type, this separation of lung is complete with the formation of an accessory, ectopic lobe enclosed in its own pleural covering and located either above or below the diaphragm.[3] In intralobar sequestration, there is partial separation of lung tissue which is contained within the visceral pleura of the affected lobe.[3] The chest roentgenogram in this type usually reveals a mass density in one of the lower lobes, and if there is communication with the tracheobronchial tree, air-fluid levels may be present.

Blood supply to the sequestered lung is from one or several systemic arteries arising from the aorta or its branches.[4] Characteristically, venous drainage in the intralobar type is by way of the pulmonary veins.[6] In the extralobar type, the venous return is to the systemic circulation, usually the azygous, hemiazygous or caval veins.[3,4] Venous drainage to the portal system is rarely encountered,[5] and to our knowledge angiographic demonstration of this condition has not been previously reported. For this reason it was considered to be of interest to describe the roentgenologic features including the angiographic findings in a child with extralobar sequestration and venous return to the portal vein.

REPORT OF A CASE

K.G. C 95969. This 6 year old child was first seen at Grady Memorial Hospital at the age of 11 months with symptoms of respiratory infection. Chest roentgenograms revealed a homogeneous triangular-shaped area of increased density visible through the left heart shadow in the region of the medial and posterior basilar segments of the left lower lobe. The child responded well to antibiotic therapy, and was relatively asymptomatic until the age of 5 years, when he developed symptoms of pneumonia. Chest roentgenograms (Fig. 1, *A* and *B*) again showed the paravertebral soft tissue density with a lobulated shape on the lateral roentgenogram (Fig. 1*B*), which was essentially unchanged since the first roentgen examination. A barium swallow study (Fig. 2) revealed the esophagus to be deviated to the right in its medial third. No communication of the esophagus with this retrocardiac density could be demonstrated. Because of the possibility of bronchopulmonary sequestration the child was admitted for further roentgenologic studies.

A bronchogram (Fig. 3) showed displacement and crowding of the segmental bronchi of the left lower lobe by the mass density. No communication with the tracheobronchial tree was evident. Pulmonary arteriography was performed, and the sequestered lung did not communicate with the pulmonary vasculature. Percutaneous catheter aortography (Fig. 4*A*) revealed the thoracic aorta to descend to the right of the spine. An aberrant artery arising from the abdominal aorta at the level of the celiac axis supplied the pulmonary mass through several large branches. In addition, a small branch off the left renal artery contributed to the arterial blood supply. A diffuse opacification of the pulmonary lesion was evident on the immediate roentgenograms. A delayed roentgenogram (Fig. 4*B*) showed the venous drainage to be by way of a large vessel emptying into the portal vein.

On surgical exploration through the left seventh interspace, a solid mass enclosed in its own pleura was found in the lower left chest without any connection with the left lung. The mass was removed from the surrounding structures, namely, the esophagus and vagus nerve

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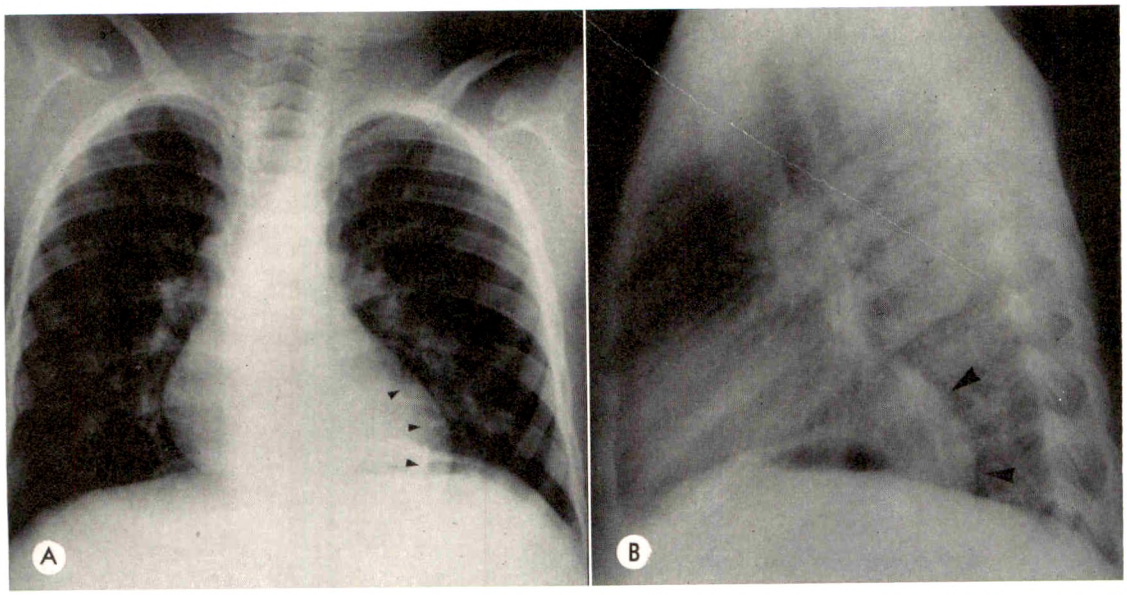


Fig. 1. (*A*) An area of increased density (arrows) representing the airless pulmonary mass is visible through the left heart shadow. (*B*) Arrows show the homogeneous mass to occupy the region of the basilar segments of the left lower lobe.

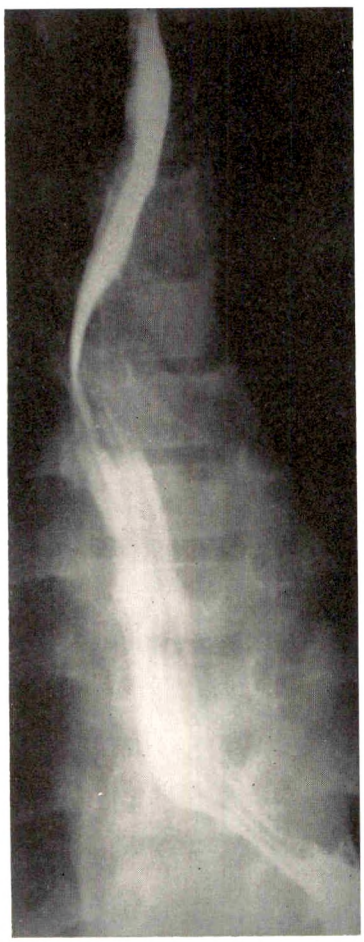


Fig. 2. Barium swallow examination shows the esophagus to be displaced to the right by the aorta. Barium does not enter the sequestered lung.

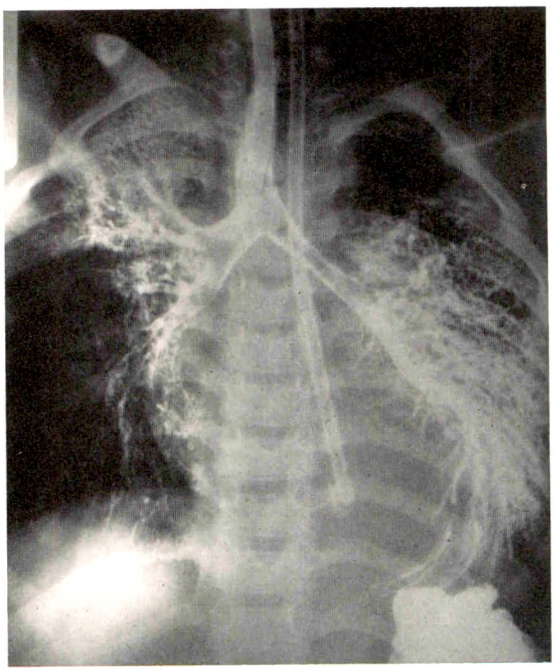


Fig. 3. Bronchogram shows no communication of the pulmonary mass with the bronchopulmonary tree. Segmental bronchi to the left lower lobe are displaced by the mass.

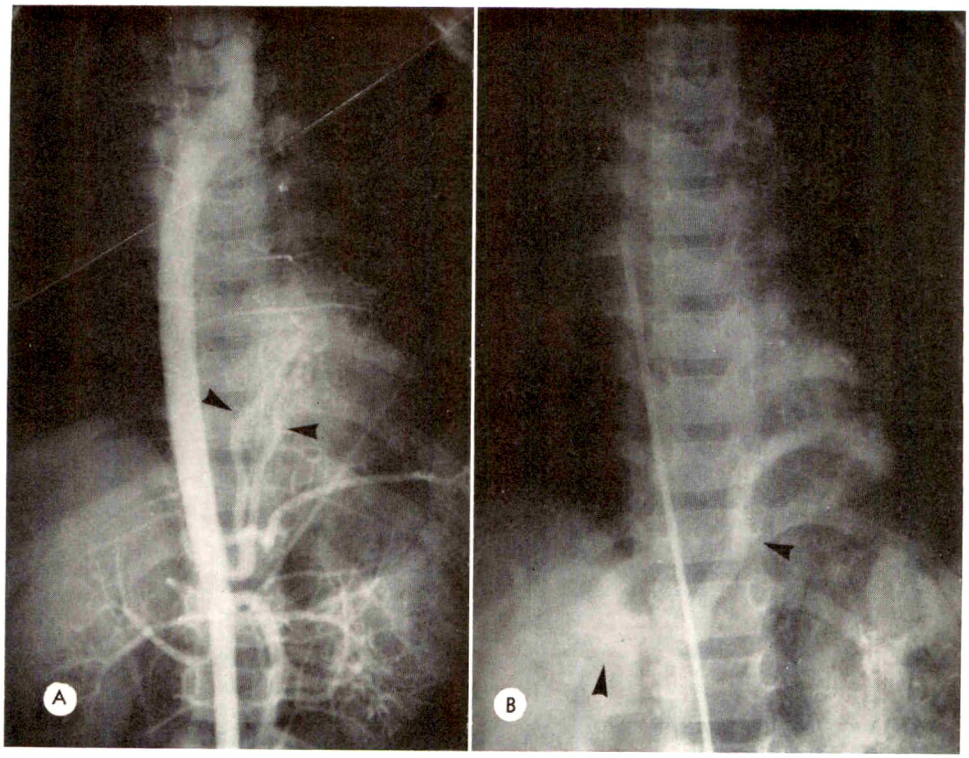


FIG. 4. (*A*) Aortogram shows a large aberrant artery from the aorta supplying the sequestered pulmonary tissue through several branches (arrows). (*B*) Upper arrow indicates a large drainage vein emptying into the portal system (lower arrow).

medially, the pericardium anteriorly, and the left lung and left diaphragm. Three large systemic arteries supplied the sequestered segment. A large vein 7 mm. in diameter drained the mass and emptied into the portal system. The postoperative course was uneventful.

On pathologic examination the tissue mass measured 7×6×5 cm. and was of reddish-blue color. Cut sections revealed soft spongy material containing multiple cystic spaces, some of which contained clear mucoid fluid. Microscopic examination showed numerous dilated bronchi and bronchioles. Very little alveolar tissue was present.

SUMMARY

The findings on the chest roentgenogram, barium swallow study, and bronchogram, together with the angiographic studies of a 6 year old child with extralobar pulmonary sequestration and venous drainage to the portal vein are presented.

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A NEW ACID MUCOPOLYSACCHARIDOSIS WITH SKELETAL DEFORMITIES SIMULATING RHEUMATOID ARTHRITIS*

By PATRICIA WINCHESTER, M.D., HERMAN GROSSMAN, M.D., WAN NGO LIM, M.D., *and* B. SHANNON DANES, M.D., Ph.D.
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THERE are several well recognized mucopolysaccharide storage diseases with characteristic roentgenographic and biochemical features.[5] This report is concerned with the preliminary delineation of a new genetically based disorder of mucopolysaccharide metabolism. The subjects are the siblings of a consanguinous marriage who presented a picture with some roentgenographic features resembling rheumatoid arthritis. There were progressive grotesque deformities of trunk and limbs, coarsened facial features, and peripheral corneal opacities. No mucopolysaccharides were found in the urine. The biochemical disorder was partially characterized by skin fibroblast tissue culture demonstrating increased cellular metachromasia of the affected siblings and their parents by the technique described by Danes and Bearn.[3] Histochemical studies showed increased intracellular uronic acid indicating that acid mucopolysaccharides are abnormally elevated in both parents and markedly elevated in the children. This is a pattern consistent with an autosomal recessive mode of inheritance with the related parents being heterozygous and the affected children homozygous for the genetic disorder.

DESCRIPTION OF THE 2 SIBLINGS

The older child (I.C. N.Y.H. # 819389) was normal at birth. Her parents are first cousins, their grandmothers being sisters. The first evidences of disease appeared at 1½ months when limitation of motion of knees and spine, proximal interphalangeal joint enlargement and bulbous painful wrists became apparent. The liver and spleen were not enlarged and the cry was normal. There were no subcutaneous nodules or rash, and fever was not conspicuous. The sedimentation rate was slightly increased, and all serologic parameters of rheumatoid arthritis were negative.

By age 3 years, the anterior fontanelle was still patent, the tongue large and the dentition delayed. At age 5 years, an ophthalmologist noted peripheral corneal opacities in both eyes, and now at age 12 years the vision is quite poor.

By age 8 years, despite intensive rehabilitative measures she exhibited extensive contractures and grotesque deformities (Fig. 1). Her facial features were coarse with gargoyle-like thick lips, hypertrophied gums, fleshy nose with a flat bridge and a prominent forehead (Fig. 2). T wave changes on electrocardiogram (ECG) suggested myocardial damage, but as yet no clinical signs of cardiac failure have been noted. No gross mental deficiency is present.

The sibling (M.C. N.Y.H. #998574), now 3½ years old, was also the product of an uneventful pregnancy and was normal at birth. Growth and development proceeded within the norms except that dentition was delayed at 12 months. From that time on feeding and weight gain became poor. By age 20 months, spine and limb stiffness developed and the facial features began to coarsen. Peripheral corneal opacities were apparent by age 24 months. Routine blood tests were normal without any evidence of an inflammatory process. Her ECG also showed ST segments and T wave abnormalities that suggested myocardial damage. In general she has been following a course similar to that of her sister.

ROENTGENOGRAPHIC FEATURES

Serial examinations of the joints of both children show progressive destructive dis-

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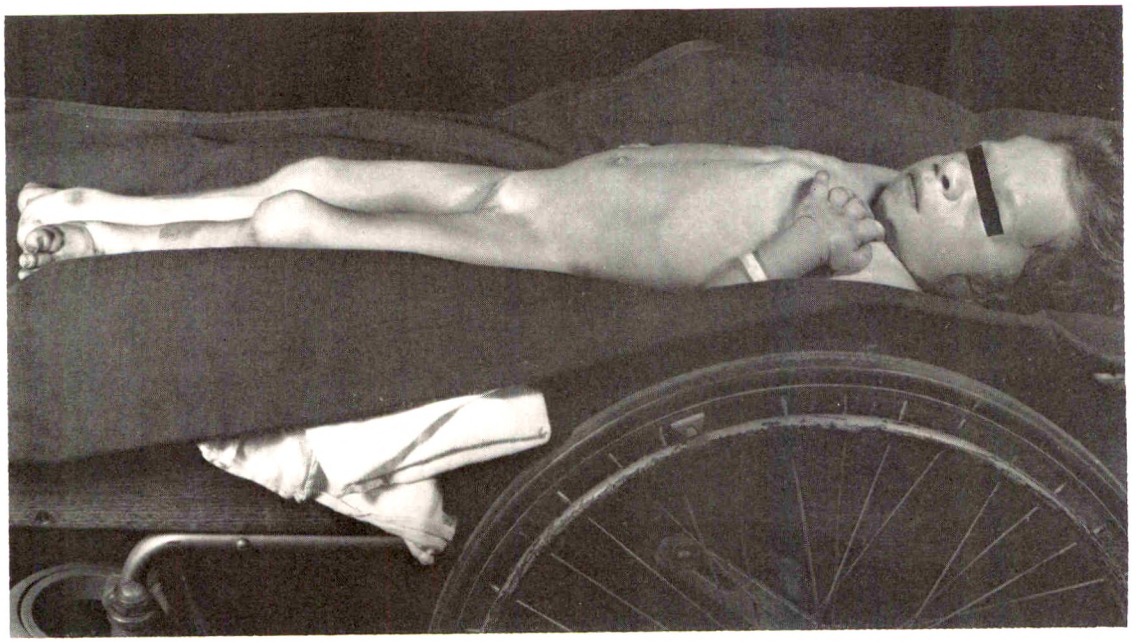


FIG. 1. Older sister, age 8 years. The deformities of the hands, knees, and feet are seen. The child is almost totally immobile.

ease. The knees of the younger sister at 20 months (Fig. 3) are osteoporotic and the periarticular soft tissues are prominent. By age $3\frac{1}{2}$ years (Fig. 4), the osteoporosis is more marked and destructive changes appear on the epiphyseal articular margins. The knees of the older sister at 12 years (Fig. 5) are ankylosed. The shafts of the long bones are markedly thinned, and the metaphyseal areas widened.

Marked destructive changes are present at the hands and wrists of the younger child. At age 20 months, osteoporosis (Fig. 6*A*) is evident. By age $3\frac{1}{2}$ years (Fig. 6*B*) a greater than normal number of small carpal centers with irregular margins appear. The older sibling's hands demonstrate the relentless progression of the process. At age



FIG. 2. Older sister, age 8 years. The facial features are coarse: prominent forehead, fleshy large nose, with a depressed bridge, thick lips.



FIG. 3. Younger sister, age 20 months. The periarticular soft tissues are prominent about the knees. The bone density is slightly decreased.

$2\frac{1}{2}$ years the early appearance of the carpal ossification centers (Fig. 7*A*) is seen, while at age 6 years (Fig. 7*B*) the carpals are destroyed and the base and proximal shaft of the metacarpals are beginning to disappear. In addition, the phalanges from age 6 years onward are expanded with a coarsened cystic trabecular pattern (Fig. 7*C*). Bone resorption is noted in the distal phalanges of the fifth finger by age 8 years. Similar destructive changes are present in the ankles and feet. At age 12 years, the long bones of the upper limbs (Fig. 8) are thin and bone erosion is present in both elbows and shoulders. Flaring of the metaphysis of the distal radius and proximal humerus is prominent.

Subluxation of C1 on C2 occurred in both siblings (Fig. 9). Roentgen studies of the skull show delayed closure of the anterior fontanelle (Fig. 10), widely open sutures, prominence of the frontal region, flat mandibular condyles and delayed tooth eruption.

During the first 2 years of life, roentgenograms of the chest and pelvis are normal but by age 12 years extreme deformity is present. There is a kyphoscoliosis (Fig. 11) of the thoracolumbar spine. The ribs do not flare, but the clavicles appear expanded and their distal ends are resorbed. The hips (Fig. 12) and pelvis are misshaped. The left femoral head appears totally destroyed and the right ischium and pubis are rotated and appear elongated. The right ilium is square.

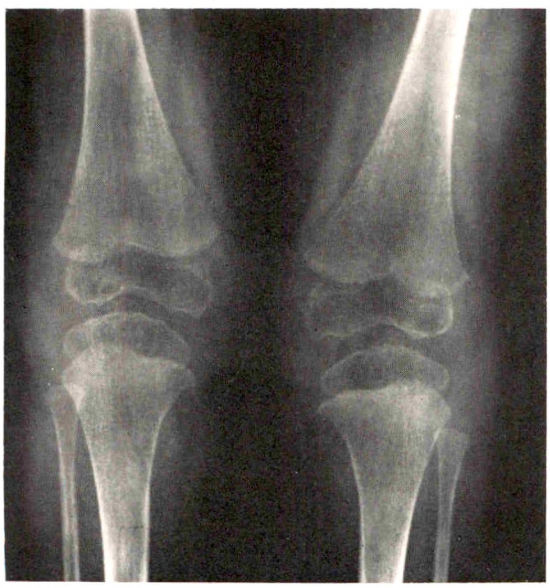


Fig. 4. Younger sister, age $3\frac{1}{2}$ years. Irregularities of epiphyseal centers, osteoporosis, and advanced maturation are observed.

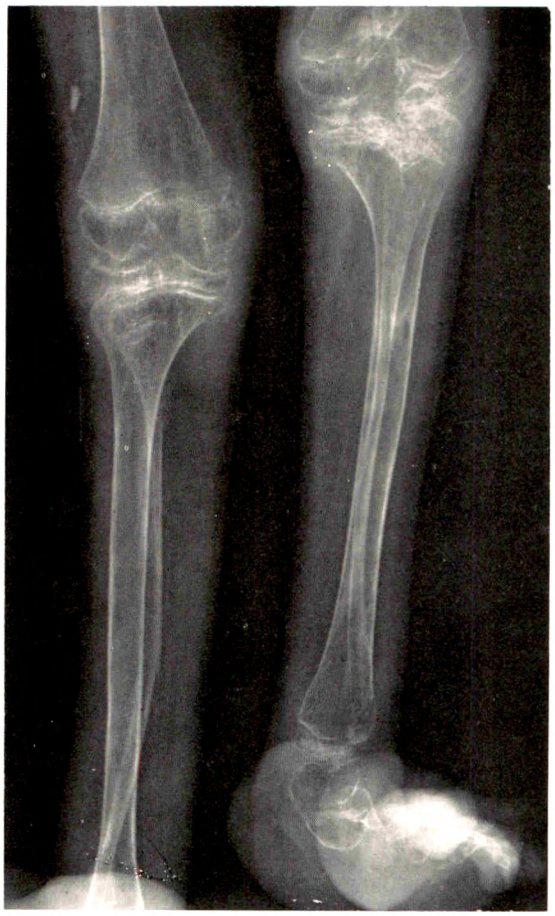


Fig. 5. Older sister, age 12 years. The knees are ankylosed. The ends of the long bones are flared. The bone density is markedly diminished. The left distal fibula is eroded. Destruction of the small bones of the foot is seen.

DISCUSSION

There are a limited number of diseases, certain of them quite rare, that share some features with the syndrome described herein. The roentgenographic findings of destructive joint disease in their early stage are suggestive of severe juvenile rheuma-

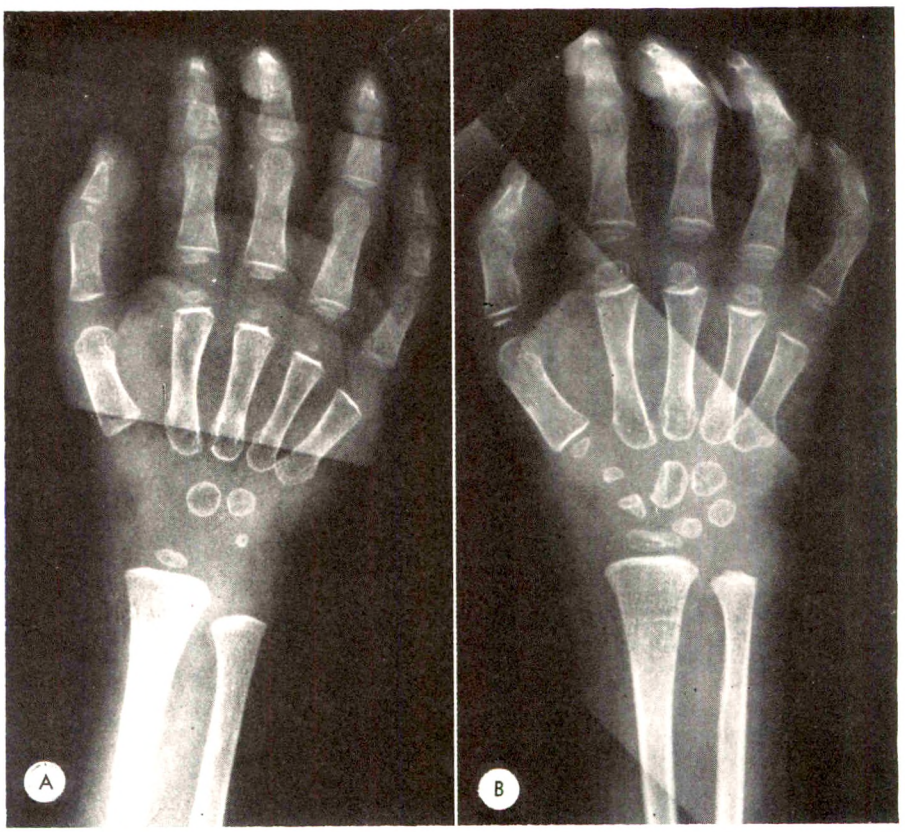


FIG. 6. (*A*) Younger sister, age 20 months. The epiphyseal centers appear normal. (*B*) Younger sister, age $3\frac{1}{2}$ years. The carpal centers demonstrate irregular destruction. The medullary canal of the proximal phalanges is slightly expanded.

toid arthritis. However, the clinical setting is not that of Still's disease. In the sisters described the dominant joint findings were pain and deformity with only minimal signs of inflammation and heat. At no time was there an elevation of erythrocyte sedimentation rate or significant fever. Involvement of the eyes is encountered in rheumatoid arthritis. Keratoconjunctivitis sicca, anterior nongranulomatous uveitis and scleromalacia perforans, with marginal furrows usually in the inferior cornea have recently been described.[2a] In both these children the cornea was clouded peripherally. A biopsy of the younger child's cornea showed no granuloma.* As the bone deformities evolve they demonstrate a number of features not seen in rheumatoid arthritis. The bones of the hands and feet are expanded with coarsened trabecular patterns, and the metaphyses of the long bones are flared.

The relationship of this syndrome to the other well known mucopolysaccharide storage diseases must be considered. In common with the most frequently encountered mucopolysaccharidoses are the histochemical findings of metachromasia and high uronic acid content of the skin fibroblast culture, the clinical features of peripheral corneal opacities, coarse facial appearance, and skeletal and articular abnormalities. Each mucopolysaccharidosis, the Hurler, Hunter, Sanfillippo, Morquio, Scheie and Maroteaux-Lamy syndromes, as summarized by McKusick,[5] has its unique symptomatology, but joint disturbances are encountered in all. In most, this is periarticular with ligamentous and tendon involve-

* The eye findings are to be presented by Dr. S. I. Brown in a separate communication.

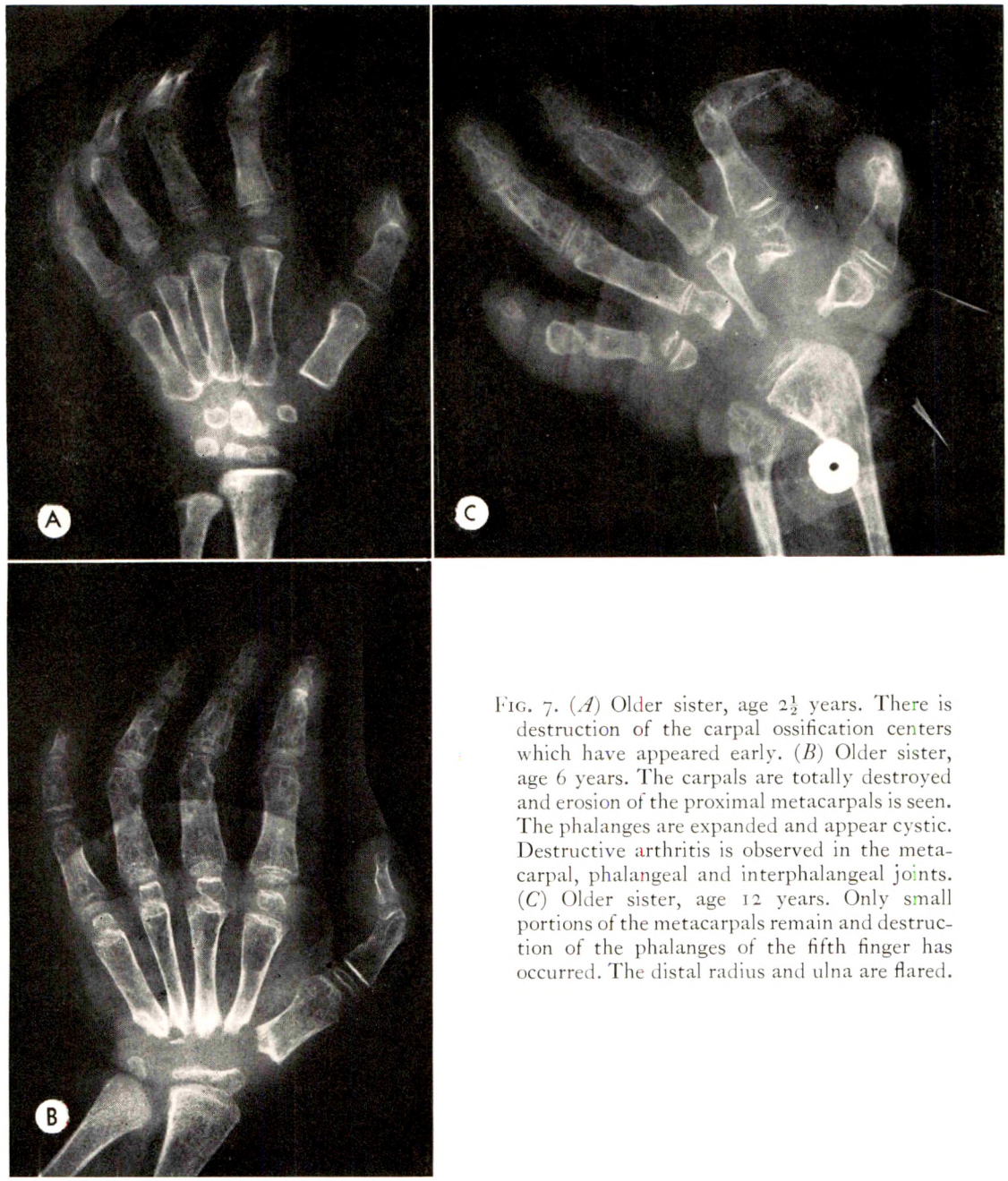


Fig. 7. (*A*) Older sister, age 2½ years. There is destruction of the carpal ossification centers which have appeared early. (*B*) Older sister, age 6 years. The carpals are totally destroyed and erosion of the proximal metacarpals is seen. The phalanges are expanded and appear cystic. Destructive arthritis is observed in the metacarpal, phalangeal and interphalangeal joints. (*C*) Older sister, age 12 years. Only small portions of the metacarpals remain and destruction of the phalanges of the fifth finger has occurred. The distal radius and ulna are flared.

ment. In this group, Farber's syndrome and Scheie's syndrome are distinctive because of the degree of joint involvement. The principal findings in Scheie's syndrome[6] are peripheral clouding of the cornea, stiff joints without roentgenographic bone findings, aortic regurgitation and survival to a late age. Chondroitin sulfate B is excreted in the urine in excess.

Farber's disease is characterized in part by destructive arthritis and increased tissue mucopolysaccharide.[1,2] The clinical manifestations appear soon after birth with tender joints, periarticular swellings, hoarse cry, and respiratory distress. Nodular tumefactions develop about joints and hyperpigmentations occur over the dorsal joint surfaces. The joints become fixed by



FIG. 8. Older sister, age 12 years. Extensive destruction of elbow is seen. The metaphyseal regions of the proximal humerus and distal radius are widened.

contractures. Facial features are described as apathetic and similar to cretins. No corneal opacities have been noted, but granulomas have been described in the conjunctiva. In all cases but one,[2,8] there has been severe mental retardation and a progressive course leading to death within the first 2 years secondary to respiratory infection. The roentgenographic findings in Farber's disease are marked periarticular soft tissue swelling, juxta-articular bone erosion, and periosteal reaction.[7] Thus in Farber's disease the joint abnormalities are predominantly periarticular with involvement of adjacent bone, whereas in the siblings described the abnormality is of a different nature, being particularly an intra-articular destruction with resorption of small bones of the joints and portions of the neighboring long bones.

In 1949, François described an extremely rare storage disease with deformity of



FIG. 9. Older sister, age 12 years. There is a subluxation of C1 forward on C2.

joints.[4] He advanced evidence of storage of lipid in foam cells from subcutaneous nodules. The disorder occurred in 2 siblings of normal intelligence and was characterized by widespread xanthomata involving the skin of the neck, pinnae, and extensor surfaces of the wrists and fingers, subepithelial opacification of the cornea peripherally and centrally and symmetric bone deformities localized to the distal extremities. The roentgenograms of the hands and feet showed both early appearance and later destruction of the round bones of the wrists and feet. Subluxations of the metatarsal phalangeal and metacarpal phalangeal joints occurred with irregularities in the metacarpal and tarsal heads. No other joints were abnormal and the facial features were normal.

SUMMARY

Two siblings are described with biochemical evidence of mucopolysaccharide storage presumably inherited as an autosomal recessive.

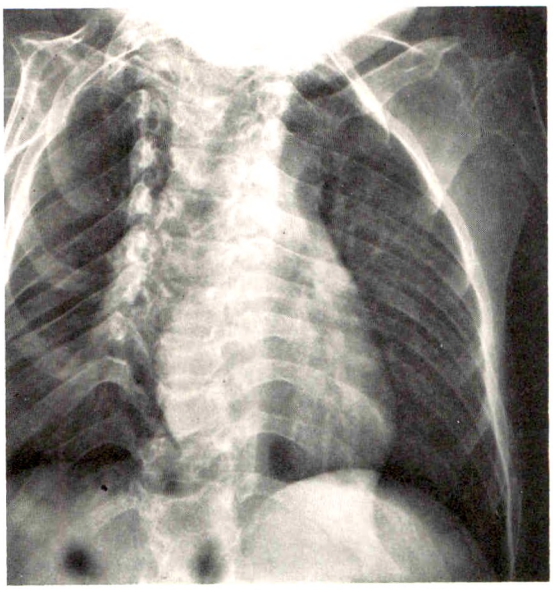


Fig. 11. Older sister, age 12 years. Mild scoliosis of the dorsal spine is seen on supine roentgenogram. The clavicles are widened with destructive change at the acromial junctions. The ribs are not unusually flared. The heart size is normal.

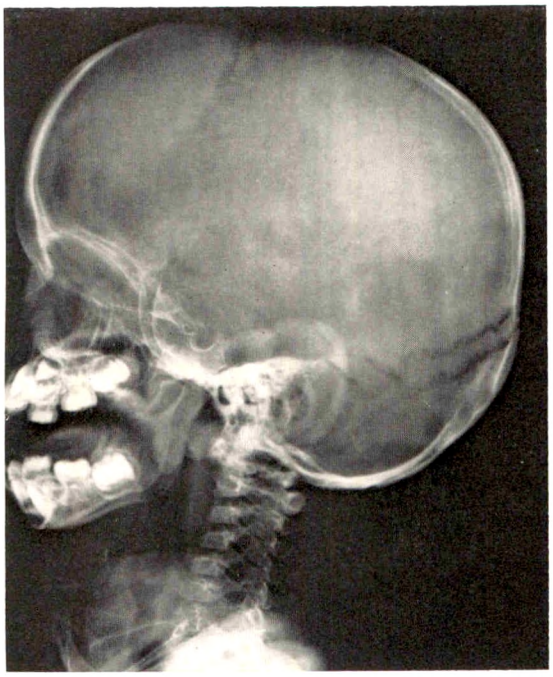


Fig. 10. Younger sister, age $3\frac{1}{2}$ years. The anterior fontanelle is opened. The sutures are prominent. The sella turcica is omega shaped. The mandibular condyles are flat and the dentition is delayed. Subluxation of C1 is seen.



Fig. 12. Older sister, age 12 years. The bone density is decreased. The femoral head is totally destroyed, the right is very flat. Coxa valga is present. The left acetabulum appears displaced superiorly. The entire left pelvis is rotated with apparent elongation of the pubis and ischium. The right ilium is squared.

The syndrome is characterized by a progressive grotesque deformity due to intra-articular destruction. There are coarsened facial features and peripheral corneal opacification. Mucopolysaccharide is not excreted in abnormal amounts, and mental retardation is not present.

The differentiation from rheumatoid arthritis and recognized mucopolysaccharide storage diseases is discussed.

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SKULL EROSION COMPLICATING TRAUMATIC PORENCEPHALY IN INFANCY*

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MANY different interpretations exist regarding the definition of the term porencephaly, first described in 1859 by Heschl.[6] The definition of porencephaly as "a defect communicating with the ventricles or separated from them by a thin layer of brain tissue and covered on the outside by arachnoid," was proposed by LeCount and Semerak.[8] This definition is generally accepted and will be so used in this discussion.

Porencephalic cysts may be congenital or acquired. The pathogenesis of acquired porencephaly is varied and may result from the destruction of cerebral tissue by trauma, localized vascular insufficiency, inflammation or degenerative processes.

Courville[3] observed that the immature infant brain was susceptible to cavitation and that this tendency diminished with age. The progressive development of porencephalic cysts in areas of cerebral softening and hemorrhage in infants with birth trauma was described in 1927 by Schwartz[10] following a comprehensive study. Jaffé[7] noted that porencephaly occurred more frequently in infants who were premature or the product of a prolonged labor or an instrumental delivery. Since then only a few cases of post-traumatic porencephalic cysts in infancy have been recorded. In the series of porencephalic cysts reported by Drew and Grant,[4] only 2 of the 30 cases were in this category and in 2 other series the incidence was only 2 in 22[3] and 1 in 32.[9]

In 1965 Barrett and Mendelsohn[1] reported 3 unusual cases of post-traumatic porencephaly in infancy. In an 8 month old infant with meningitis a large intracortical hematoma developed, secondary to the trauma of repeated subdural taps, and proceeded to porencephalic cyst formation. They speculated regarding the incidence of traumatic porencephalic cyst formation secondary to a hemorrhagic loss of brain substance following subdural and ventricular punctures and indicated that this complication might occur more commonly than recognized, since the location of such cysts is predominantly in the frontal lobes where large lesions may be present with only minimal clinical findings.[4,10]

The purpose of this paper is to briefly review the pathogenesis of traumatic porencephaly in infancy and to present a case with skull erosion as an unusual complication.

REPORT OF A CASE

P.E., a 4 month old infant, suffered a head injury in an automobile accident on December 30, 1965. On admission to hospital elsewhere she was drowsy but reacted to stimulation by crying. Skull roentgenograms demonstrated a 3 cm. linear fracture in the anterior portion of the left parietal bone and a 4 cm. fracture in the right parietal bone posteriorly (Fig. 1). Some 8 hours later she developed left-sided seizures. Bilateral subdural taps were performed and a small amount of serosanguineous fluid was recovered from the right side. She was transferred to the University of Minnesota Hospitals on December 31, 1965, where a left hemiparesis developed shortly after admission. Bilateral subdural taps were negative. The following day she became less responsive and clonic twitching of the right extremities developed. Again, bilateral subdural taps were performed but no fluid was obtained from either side. Several blood transfusions were given because of extensive subgaleal bleeding. She gradually improved without further treatment and was discharged on January 19, 1966. Subsequent outpatient examinations at 6 months of age and again at 8½ months of age

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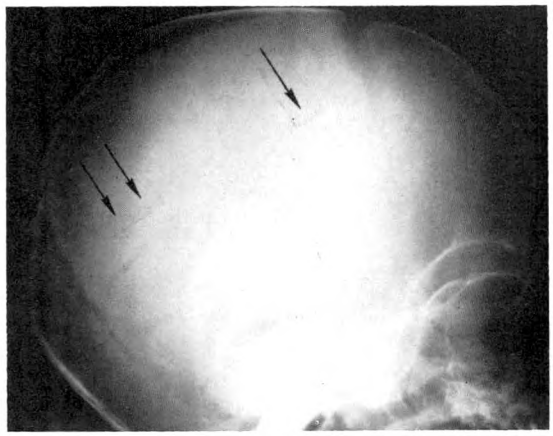


FIG. 1. Skull roentgenogram at age 4 months demonstrates a left anterior parietal fracture (single arrow) and a right posterior parietal fracture (double arrows). Note normal anterior fontanelle region.

indicated an excellent recovery with no neurologic sequelae.

On June 30, 1966 at age 10 months, she suffered a minor head injury and skull roentgenograms were taken at The Children's Hospital, St. Paul. These revealed a large midline bone defect in the region of the anterior fontanelle (Fig. 2, *A* and *B*), which was not present on the skull roentgenograms taken at the time of the original injury 6 months previously. The edges of this calvarial defect were everted, strongly suggesting an underlying superficial mass. Pressure from a contiguous arachnoidal cyst was suspected and surgical exploration was performed at the University of Minnesota Hospital on August 2, 1966. Because of adhesions, the meninges could not be individually identified but no arachnoidal cyst was present. The brain was adherent to the periosteum-galea in the area of the skull defect and contained multiple superficial intracerebral cysts on the right side and a single large intracerebral cyst on the left side. Each of the cysts contained xanthochromic fluid but there was no communication between them and either the subarachnoid space or the ventricular system. Treatment was effected through establishment of a surgical communication between the bilateral cysts and the corresponding lateral ventricles. The child's subsequent course and development have been uneventful.

DISCUSSION

The bilateral porencephalic cysts which developed in the 6 month period following severe head trauma in this infant were unusual in that they produced pressure erosion and eversion of the overlying skull. This phenomenon can occur only when a cystic lesion is sufficiently close to the surface of the brain to transmit the pulsatile pressure of the ventricular fluid to the overlying vault. The reduced resistance of the still patent anterior fontanelle to the contiguous porencephalic cysts was probably a significant factor in the rapid

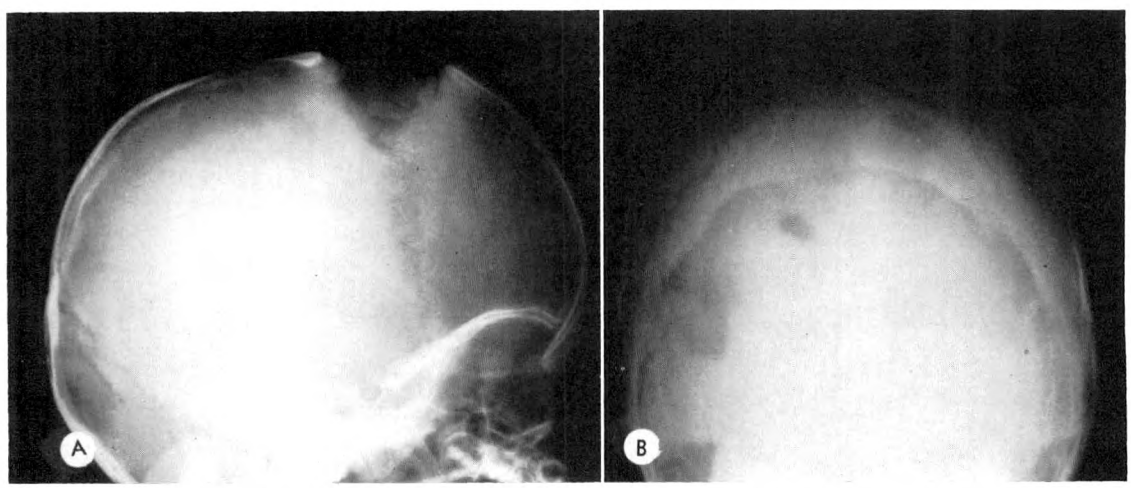


FIG. 2. (*A*) Lateral skull roentgenogram at age 10 months reveals a large calvarial defect in the region of the anterior fontanelle. The fractures have healed. (*B*) Towne view demonstrates the extensiveness of the bone defect produced by the underlying intracerebral cysts.

development of the large skull defect at this site. The majority of porencephalic cysts are located deeper within the brain substance than the cysts present in this infant and hence produce no pressure erosion of the overlying calvarium. It is interesting to note that despite the extensiveness of the bilateral porencephaly, there were no neurologic signs or symptoms and the calvarial defect was detected incidentally on a skull roentgenogram taken following a minor head injury some 6 months after the original trauma. The location of the porencephalic cysts in the relatively silent frontal lobes of the brain was probably the major factor in the absence of neurologic findings.

The high incidence of porencephaly in association with prematurity, prolonged labor and instrumental delivery noted by Jaffé[7] suggests a common etiologic factor, namely intracerebral hemorrhage. The initial clinical findings of left hemiparesis and clonic movements of the right extremities indicated severe bilateral cerebral damage and it seems logical that the preceding head injury resulted in bilateral intracerebral hematomas which subsequently became converted into porencephalic cysts. The possibility that the intracerebral hematomas could have been secondary to the repeated bilateral subdural punctures which were performed cannot be absolutely excluded. However, the presence of neurologic signs of severe cerebral damage prior to the performance of the subdural taps makes this mechanism unlikely. The possibility of congenital porencephaly can be excluded by the normal appearance of the anterior fontanelle region in the skull roentgenograms taken at the time of the original injury. The location of the defect at some distance from the sites of the parietal fractures and the operative findings ruled out any possibility of leptomeningeal cyst formation.

CONCLUSION

Several considerations regarding traumatic porencephaly in infancy and childhood merit emphasis. Although the commonly performed procedure of subdural puncture in infants is rightfully assumed to be innocuous, it can be complicated by porencephalic cyst formation should the aspirating needle penetrate the cerebral cortex and produce an intracerebral hematoma.[1] Most traumatic porencephalic cysts produce no clinical findings initially, but slow progressive enlargement of the cyst may occur and cause seizures many years later, at which time the etiology may go unsuspected.[4,5] Hence, prompt evacuation of large traumatic intracerebral hematomas may be advisable to minimize brain damage and the likelihood of subsequent porencephalic cyst formation. Should such a cyst form, early drainage into the ventricular or subarachnoid system may be indicated to prevent progressive enlargement.

SUMMARY

The development of extensive skull erosion as an unusual complication of bilateral traumatic porencephaly in an infant is described.

The pathogenesis, clinical manifestations and treatment of this condition are briefly discussed.

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CELLULITIS WITH UNDERLYING INFLAMMATORY PERIOSTITIS OF THE MANDIBLE*

By MELVIN J. SUYDAM, M.D., *and* VICTOR G. MIKITY, M.D.
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PERIOSTEAL new bone formation can be caused by a variety of neoplastic, metabolic, traumatic and inflammatory conditions including osteomyelitis.

It is not widely known that cellulitis involving soft tissues overlying bone can cause periosteal new bone formation without there being actual infection of the bone itself.

Three cases are reported to illustrate this.

REPORT OF CASES

CASE I. G.B., a 17 month old white female, was admitted to the Los Angeles County-U.S.C. Medical Center on May 13, 1968 with a 2 week history of swelling in the left submandibular area which was clinically thought to be an abscess. Incision and drainage produced pus which on culture grew out *Staphylococcus aureus*, coagulase positive. Following treatment with intravenous methecillin, the abscess resolved. Initial roentgenograms of the mandible on May 13, 1968 (Fig. 1) revealed periosteal new bone along the body of the mandible on the left side. Roentgenograms of the clavicles, right mandible, extremities and pelvis were normal without evidence of periosteal new bone, indicating that the periostitis was not due to some systemic disorder such as Caffey's disease. Subsequent roentgenologic examinations revealed a slight increase in the density of the periosteal new bone. The most recent roentgenograms on October 2, 1968 (Fig. 2) showed the presence of dense, smooth periosteal new bone. At no time was there any radiologic evidence of destruction of the cortex or medulla of the mandible. At the patient's most recent clinic visit on October 9, 1968, she was completely well with no evidence of residual inflammatory changes in the soft tissues of the left jaw.

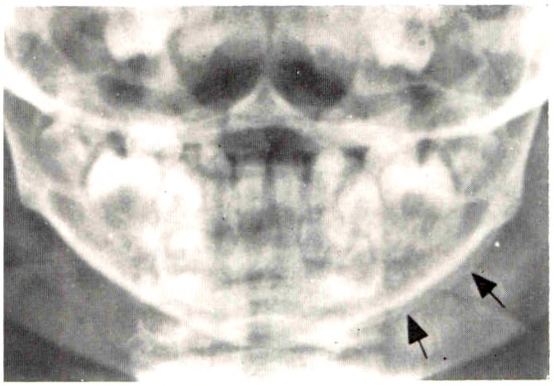


FIG. 1. Case I. Roentgenogram taken on May 13, 1968 shows faint periosteal new bone along the left side of the mandible.

CASE II. A.G., a 3 month old Mexican female, was admitted on October 17, 1968 with a history of swelling of the right side of the jaw and fever for 4 days. Clinically, the patient was thought to have an abscess. Incision and drainage produced pus, which on culture grew out *Staphylococcus aureus*, coagulase positive. The patient was treated with oral cloxacillin. Roentgenograms of the mandible on October 30, 1968 (Fig. 3) revealed periosteal new bone along the body of the mandible on the right with no evidence of actual bone destruction. Roentgenograms of the clavicles, left mandible, extremities

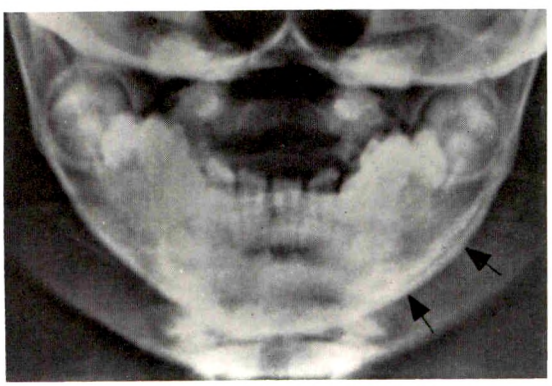


FIG. 2. Case I. Roentgenogram taken $4\frac{1}{2}$ months later shows dense smooth periosteal new bone with no evidence of bone destruction.

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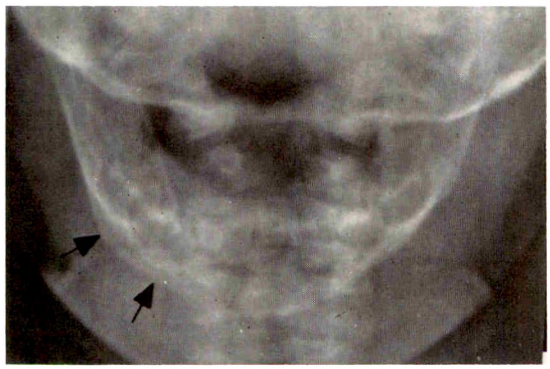


FIG. 3. Case II. Roentgenogram taken on October 30, 1968 shows periosteal new bone along the right side of the mandible. Within 1 week after this roentgenogram was taken, the patient was completely cured clinically. Follow-up roentgenograms were not obtained.

and pelvis were normal. At the patient's most recent clinic visit on November 6, 1968, there was complete healing of the abscess with no evidence of residual inflammatory changes.

CASE III. L.C., a 1 year old white male, was admitted on November 20, 1967 with a 10 day history of fever and swelling of the left side of the jaw. The patient was thought to have a cellulitis without abscess formation. Roentgenograms of the mandible, clavicles, extremities and pelvis on October 20, 1967 were normal. Following treatment with oral penicillin, the soft tissue swelling resolved and the patient became clinically well. Subsequent roentgenograms of the mandible on December 22, 1967 (Fig. 4) showed periosteal new bone along the body of the mandible on the left. The most recent roentgenographic examination on February 23, 1968 (Fig. 5) showed almost complete disappearance of the periosteal new bone. The patient was clinically well at the time of the latest roentgenographic examination.



FIG. 4. Case III. Roentgenogram taken on December 22, 1967 shows periosteal new bone along the left side of the mandible.

DISCUSSION

The first case reported here was originally thought by the admitting physician to have a soft tissue abscess with underlying osteomyelitis because of the presence of periostitis. Accordingly, the patient was admitted to the hospital and treated with intravenous antibiotics. However, because the cortex of the bone remained intact on several examinations and because there were never any lucent areas in the medullary cavity suggesting bone destruction, there was almost certainly no actual infection of the bone itself. The periosteum adjacent to the areas of cellulitis was stimulated by the adjacent inflammation to lay down new bone.

The second and third cases were treated with oral antibiotics with complete clinical cure. In these also there was never any roentgenologic evidence of bone destruction in the mandible.

Periosteal reaction in the mandible adjacent to a soft tissue infection can occur without evidence of osteomyelitis. The ab-



FIG. 5. Case III. Follow-up roentgenogram on February 23, 1968 shows that the periosteal new bone has almost completely disappeared, having been incorporated into the cortex of the growing mandible.

sence of bone destruction indicates that the bone itself is not infected, often obviating the need for hospitalization and treatment with intravenous antibiotics. Many of these patients can probably be treated with oral antibiotics as outpatients.

Other causes of periosteal new bone formation, such as Caffey's disease, hypervitaminosis A, syphilis, leukemia and metastatic neuroblastoma, should cause no problem in differential diagnosis. These disorders almost always involve more than one bone and are not associated with localized soft tissue infection.

SUMMARY

Three cases of cellulitis of the soft tissues of the jaw with underlying inflammatory periostitis of the mandible are reported. This reactive periostitis should not be confused with osteomyelitis.

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CHERUBISM—HEREDITARY FIBROUS DYSPLASIA OF THE JAWS

ROENTGENOGRAPHIC FEATURES

By EUGENE A. CORNELIUS, M.D., PH.D.,* *and* JAMES L. McCLENDON, D.D.S.†
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IN 1933, Jones[10] described a previously unrecognized disease of the jaws, multilocular in its roentgen appearance, and benign in its course. This condition was observed in 4 of 5 siblings and was later transmitted by the eldest sibling to 2 of his 4 children.[11] This unusual disorder has become more widely known only in recent years, chiefly through further case reports in the dental literature. Although many ponderous names have been applied to this disease, we prefer Jones' term, "cherubism": it is simple, it has already attained synonymity with this entity; and the clinical appearance it implies is easily remembered.

The authors present an analysis of the roentgenographic features of cherubism, a review of the literature, and a report of 2 cases. (The genetic and pathologic aspects of these cases are the subjects of other reports.[1,13]) We believe that cherubism is probably a distinctive hereditary form of fibrous dysplasia, which primarily involves the jaws. The radiologist should assume major responsibility for the diagnosis, since the roentgenographic appearance of a typical case in childhood is diagnostic, whereas the clinical and pathologic features are less specific. The correct diagnosis is important in order to avoid unnecessary surgery and radiation therapy,[13] and to be alerted for other possible cases in the family.

REPORT OF CASES

CASE 1. A white boy $3\frac{5}{6}$ years of age was seen by a physician in June, 1947 because the foster mother suspected mumps; however, other persons had noted facial swelling for about 6 months. Physical examination prior to adoption at 8 months of age had revealed no abnormalities.

On admission to a Houston hospital on June 30, 1947, the physical signs noted were fever, nasopharyngitis, bilateral facial swelling, a high palate, and enlarged cervical lymph nodes. Routine blood and urine tests were normal. Serum calcium and phosphorus tests were within normal limits on this and on subsequent admissions. Roentgenograms revealed bilateral multilocular cystic expansion of the mandible, extending from the anterior portion of the body to the notch. In the lateral projection, a soft tissue mass was evident in the antrum. The maxillary teeth were displaced forward, exposing the posterior portion of the hard palate (Fig. 1).

During the next 3 months, both sides of the mandible and the right maxilla were curetted. The tissue obtained during these and four subsequent operations was similar in appearance: there was a fibrous stroma with numerous giant cells and small bone spicules.[13] The pathologic diagnosis was fibrous dysplasia or benign giant cell tumor.

Extensive maxillary involvement was still evident in October, 1947. Bone expansion and destruction, as well as antral soft tissue masses, were seen in both maxillae (Fig. 2).

Roentgenograms in 1948 demonstrated bone regeneration in the mandible, but by 1949 progression of mandibular and maxillary lesions was evident. A lateral roentgenogram of the jaws now demonstrated almost the entire hard palate, as a result of forward displacement of the maxillary teeth. A bone survey revealed a 1 cm. cyst-like area in the left femoral neck. The bone age was normal. The alkaline phosphatase was 26.9 Bodansky units (normal 1–5 units but higher for children). Roentgen therapy (half-value layer 0.88 mm. Cu) was given in January, 1950, through 2 lateral portals and an anterior portal. Dosage was 400 r (air) per portal in 11 days.

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In November, 1950 (aged 7 years), bulging of the anterior portion of both maxillae was noted. A large pigmented area was evident on the left thigh. Roentgenograms showed bone regeneration on the left side of the mandible (which had been curetted in 1947 and 1949), and extensive disease on the right side, as well as progression of the maxillary disease. The left maxilla was curetted. The antrum, hard palate, and alveolar process were found to be involved. The right side of the mandible was curetted in March, 1951, and the right maxilla on November 5, 1951.

Roentgenograms on November 8, 1951 (aged 8 years) showed bone destruction in the anterior portion of the right maxilla. A rounded mass, smaller than that noted previously, was still evident in the posterior portion of the left antrum. There was a thin osseous margin about the mass as well as fairly dense internal calcification. There was marked involvement of the symphysis region of the mandible; this area was curetted 4 months later. Two years later, the left maxillary mass was more heavily calcified (Fig. 3*A*). At this time the case was re-evaluated by J. R. Thomas, M.D. (Department of Pathology, Hermann Hospital, Houston) who now considered it to be a case of cherubism.



Fig. 1. Case 1. Aged 4 years. Lateral roentgenogram of the jaws. There is bilateral multilocular expansion of the mandible. The upper and lower teeth are displaced forward. About 1.3 cm. of the posterior portion of the hard palate is exposed ("hard palate" sign; lower arrow). A large soft tissue mass with a convex upper border (upper arrows) is evident in the antrum.

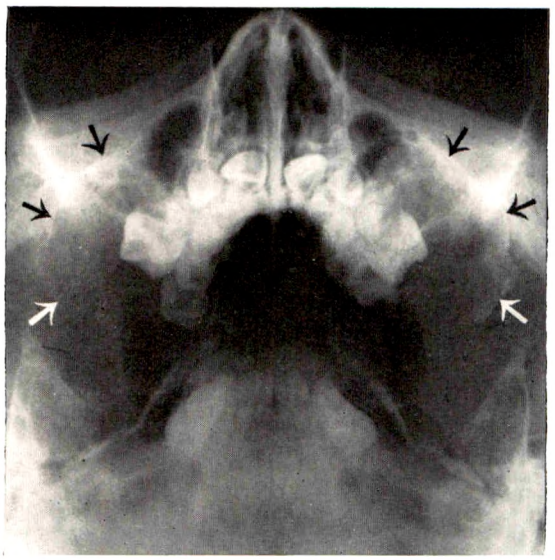


Fig. 2. Case 1. Aged 4 years. Waters' projection of the jaws. Note the antral soft tissue masses, destruction of the inferolateral antral walls, the polycyclic outline of the expanded bone near the zygomas (arrows), and the anterolateral displacement of the maxillary 6 year molars. The coronoid processes of the mandible are expanded.

In 1958 (aged 14 years), roentgenograms revealed postoperative deformities of the jaws (Fig. 3*B*). Rhinoplasty was carried out in 1959, followed by bilateral mandibular bone grafts.

Case II. A white boy, $5\frac{1}{4}$ years of age, was referred to one of us (J.L.M.) because of enlarged cervical lymph nodes and facial swelling. Bilaterally symmetrical enlargement of the mandible was present in the region of the angles. The mandibular alveolar ridge was expanded laterally, posterior to the deciduous teeth. Roentgenograms demonstrated rarefaction of the posterior portion of the body and ramus of both sides of the mandible. Intraoral dental roentgenograms revealed a unilocular area of rarefaction in the left maxillary tuberosity. A diagnosis of cherubism was made on the first examination.

The parents and 2 siblings showed no roentgenographic evidence of cherubism. An exten-

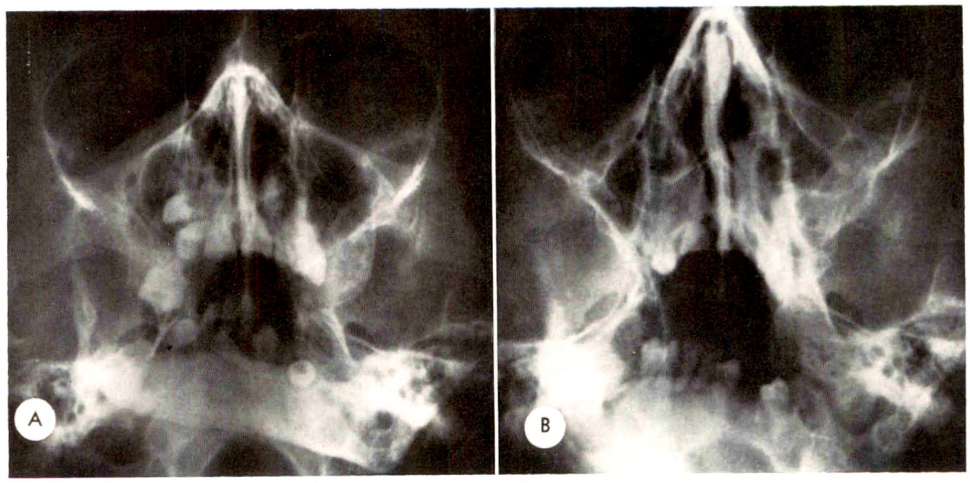


FIG. 3. Case 1. (*A*) Aged $9\frac{1}{2}$ years. Waters' projection. The partially calcified left maxillary mass is well shown. (*B*) Aged 14 years. Waters' projection. The left maxillary mass has undergone considerable regression. Both maxillae are hypoplastic, and the mandible is deformed.

sive investigation of the families of both parents disclosed no additional cases.[1,13]

At 6 years of age, the alkaline phosphatase was 8 Bodansky units. The other laboratory tests revealed no significant abnormalities. Tissue obtained from the left mandibular lesion confirmed the preoperative diagnosis. Examination 4 months later revealed enlargement of the left maxillary tuberosity and adjoining portions of the alveolar process and hard palate. A lateral roentgenogram (Fig. 4*B*) demonstrated about 7 mm. of the posterior portion of the hard palate. (A lateral cephalometric roentgenogram 9 months previously had revealed only 4 mm. of the hard palate.) The roentgenologic opinion was that bilateral posterior maxillary involvement must be present. Eleven months later the right maxillary tuberosity still did not seem enlarged clinically, but a lateral roentgenogram (Fig. 4*C*) now demonstrated 11 mm. of the hard palate. A Waters' projection showed considerable left posterior maxillary involvement and minimal expansion in the same area on the right, confirming the previous interpretation. A complete bone survey revealed defects in 4 ribs.[13]

Roentgenograms at $14\frac{1}{2}$ years revealed multilocular rarefaction of the mandibular rami and angles bilaterally, but with heavy septa. Slight residual deformity was evident in the posterior portion of the left maxilla.

ETIOLOGY

A genetic analysis of the previously reported cases of cherubism seems to indicate that this condition is a hereditary fibro-osseous disease which primarily involves the jaws. It is transmitted generally as a dominant characteristic, with incomplete penetrance in females.[1,13]

INCIDENCE

Cherubism is uncommon. Including the 2 cases herein reported, some information was available on a total of 91 cases. The disease occurs more frequently in males.[1] No ethnic predilection has been observed.[1]

CLINICAL FINDINGS

Most of the cases were detected from the second to the fifth years of life. (In 4 of the reported cases, however, an abnormality of the jaws was undoubtedly present, although not evident clinically, during the first year.[4,7,12]) Facial swelling was the initial abnormality noted in most of the cases. Loss of teeth, noneruption of permanent molars, and examination of relatives of patients with the disease were the means of detection in other cases. A classical case has a cherubic appearance due to the fullness of the cheeks. The greatest expansion of the jaw bones probably occurs within the first few years of onset. Spontaneous improvement usually begins in late child-

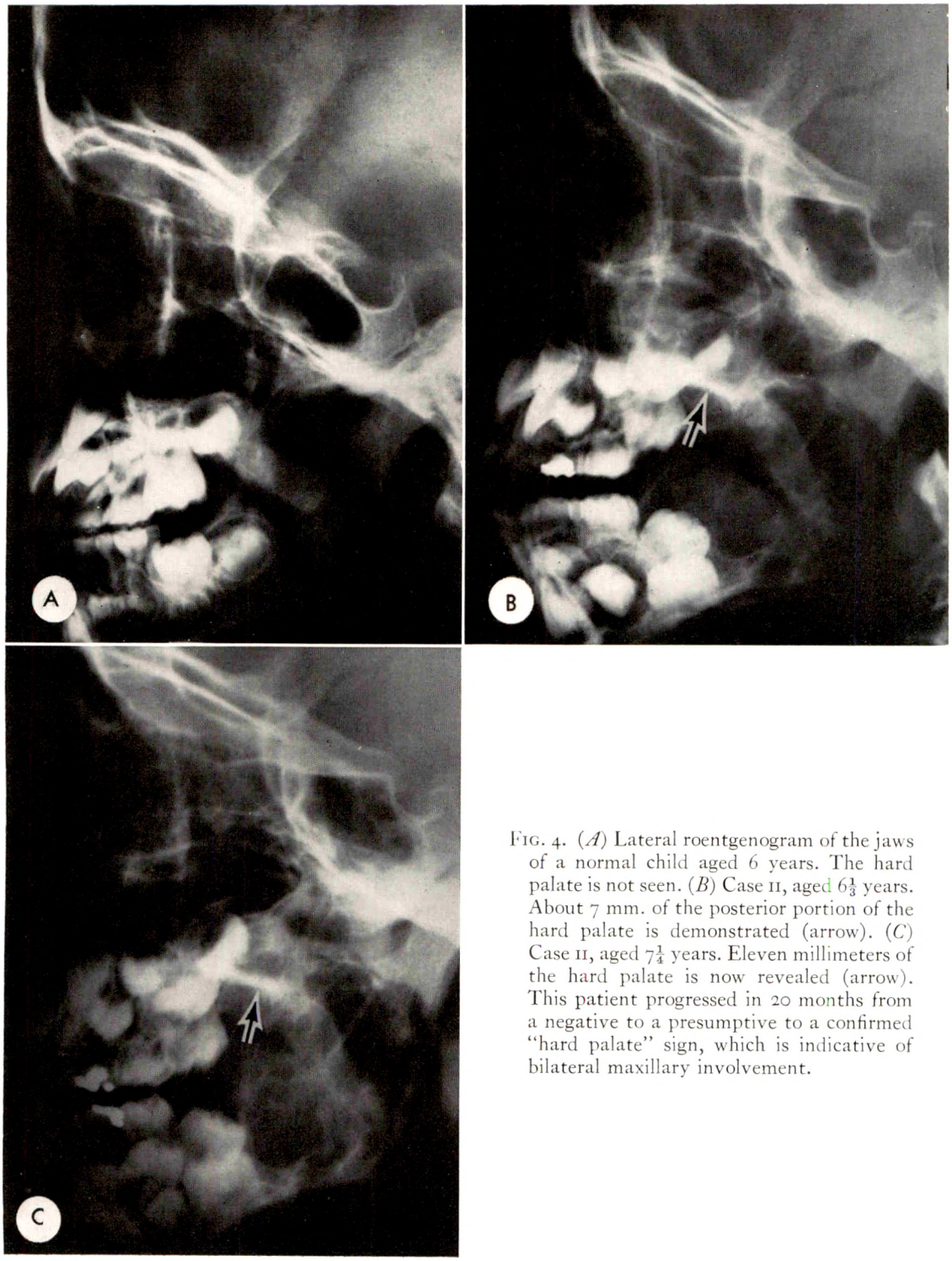


Fig. 4. (*A*) Lateral roentgenogram of the jaws of a normal child aged 6 years. The hard palate is not seen. (*B*) Case II, aged $6\frac{1}{3}$ years. About 7 mm. of the posterior portion of the hard palate is demonstrated (arrow). (*C*) Case II, aged $7\frac{1}{4}$ years. Eleven millimeters of the hard palate is now revealed (arrow). This patient progressed in 20 months from a negative to a presumptive to a confirmed "hard palate" sign, which is indicative of bilateral maxillary involvement.

hood and continues after puberty, so that by middle age there is no striking abnormality. Occasional cases may show little or no regression.

Enlarged submaxillary lymph nodes were present in most of the patients first seen at 6 years of age or younger, but gradual regression occurred in older children. Histologic examination has revealed reticuloendothelial hyperplasia, prominent germinal centers in the lymphoid tissue, and fibrosis.[8,10,17] These changes may be secondary to gingival inflammation due to malposition of the teeth.[4]

Although skin pigmentation has been reported previously in 1 case,[19] Case 1 is the first patient with a large area of pigmentation characteristic of that found in fibrous dysplasia. We believe that this is a significant finding.

Routine blood and urine examinations, and serum calcium and phosphorus values were normal. Abnormally high alkaline phosphatase values were recorded in some cases of cherubism; this is a well-known finding in fibrous dysplasia.[15]

ROENTGENOGRAPHIC FINDINGS

The mandible typically shows bilaterally symmetric, well-defined, multilocular areas of radiolucency extending from the molar region to the notch. (Unilateral mandibular disease, with roentgenographic proof, has been observed in 3 cases.[11,18,19] The diagnosis in these cases depended on the demonstration of bilateral involvement in the relatives.) Bone expansion is present. The cortex is thin and occasionally it is absent.

The molar and retromolar region and the adjoining anterior portion of the ramus are probably the initial sites of involvement. With further growth of the lesions, the anterior portion of the body and the entire anteroposterior width of the ramus are affected. The condyles are the only portions of the mandible which are not involved.

The major destructive changes in the mandible occur during the first few years of the disease. Beginning at 8 to 12 years, the bone septa increase in density. New cortical bone is laid down and the margins of the mandible become more regular. Spontaneous regression may be evident in the posterior portion of the mandible while active growth is occurring simultaneously in the anterior portion. In adults, the multilocular pattern is usually poorly defined or absent, and the entire mandible may appear sclerotic.

Maxillary involvement is less frequent and usually is less extensive, and does not occur in the absence of mandibular disease. The tuberosity and adjoining molar region are first involved, corresponding to the initial site in the mandible. More extensive lesions involve the alveolar processes and encroach on other bone structures. Because of the paucity of spongy bone in the maxilla most cases show cortical expansion, destruction, and the presence of soft tissue masses in the oral cavity, canine fossa, and antrum. With regression, calcification of the tumor may occur. In most adults who have had the disease, the maxillae appear normal.

The characteristic appearance of maxillary disease, as seen in the lateral projection, was well demonstrated in the 2 cases described in this report. A rounded soft tissue mass may be evident in the posteroinferior portion of the antrum. The dental follicles in the posterior portions of the maxillae are absent or displaced forward and upward, further defining the mass and exposing the posterior portion of the hard palate ("hard palate" sign) (Fig. 1; and 4, *B* and *C*). This sign is readily detected and is useful in determining the presence, extent and growth of maxillary foci. Lateral roentgenograms of the skulls of 290 children up to 15 years of age, chosen at random, were reviewed for comparison (Fig. 4*A*; Table 1). It was concluded that in a child with cherubism, demonstration of more than 5 mm. of the posterior extremity of the hard palate is presumptive evidence of maxillary disease.

Dental agenesis, incomplete develop-

ment or resorption of roots, displacement of teeth and follicles, sloughing of teeth, and noneruption of teeth were noted. The effects on the dentition appear to be due to the physical presence of the abnormal tissue.

Lesions noted elsewhere in the skeleton in individual cases were coxa plana,[4] a histologically proven focus of fibrous dysplasia in the upper humerus,[2] defects in the anterior ends of the ribs[23] (Case 1), a multilocular area in the triquetrum bone bilaterally,[18] and a cyst-like area in the upper femur (Case 1).

DIFFERENTIAL DIAGNOSIS

The roentgenographic features in a typical case are diagnostic. Biopsy may be of little value, since the histologic appearance is nonspecific and cannot be differentiated with certainty from that seen in fibrous dysplasia, giant cell reparative granuloma, giant cell tumor, and the localized bone lesions of hyperparathyroidism.[22]

A number of conditions may simulate cherubism clinically, but are distinguished by the absence of intraosseous disease. These include bilateral parotid enlargement (*e.g.*, mumps), benign masseteric hypertrophy, and fibromatosis gingivae.[14] Bilateral dentigerous or primordial cysts could resemble cherubism clinically, but occur in older patients.[5]

The relationship of cherubism to fibrous dysplasia has been the subject of much controversy. Although some authors make no distinction between the two conditions, there are definite differences. Fibrous dysplasia is not hereditary. Females are more frequently affected. Sexual precocity is frequently present.[15] The distribution in the jaws is not bilaterally symmetric, and the maxilla is more frequently affected.[24] If polyostotic, it tends to be unilateral. It becomes evident clinically at a slightly older age than cherubism. Facial deformity does not decrease with age, and may actually increase, even in old patients.[24] On the other hand, some features of cherubism indicate a close relationship to fibrous dysplasia. These include the general age distribution, the histologic appearance, the roentgenographic appearance of the individual foci, and the progressive calcification of some lesions. Histologically and roentgenographically, the late stages of cherubism may be identical with fibrous dysplasia.[4] The presence of skin pigmentation in 2 cases of cherubism, and of bone lesions outside the jaws in 4, both of a type which occurs in fibrous dysplasia, seems definite evidence of the close relationship of the two diseases. Cherubism might be considered as a distinctive hereditary form of fibrous dysplasia, which primarily involves the jaws.

Infantile cortical hyperostosis may affect siblings, but it occurs at an earlier age than cherubism and is characterized by cortical thickening of the mandible, without loculation.[3]

Ameloblastoma is unicentric and the roentgen appearance differs from that of cherubism. The tumor is rounded, locules of varying size are present, and crenated bone fragments may be present internally

Table I

HARD PALATE SIGN IN NORMAL CHILDREN

Age (yr.)	No. of Cases	Per cent Positive	Range of Length of Hard Palate (mm.)
0–1	10	70	4–15*
1	10	70	2–3
2	10	30	2–4
3	20	55	2–5
4	50	48	1–5
5	50	38	1–4
6	50	22	1–4
7	10	20	1–2
8	10	10	2
9	10	20	2
10	10	40	2–3
11	10	20	3–6
12	10	20	3
13	10	10	10
14	10	20	3–4
15	10	50	2–6

* Accurate evaluation difficult in this age group.
In 4 cases with congenital absence of the maxillary third molar follicles, 6–10 mm. of the hard palate was exposed.

and at the periphery.[5] Cases of minimal unilateral cherubism may not be differentiable from unilocular or polycyclic ameloblastoma by the roentgenographic appearance alone, but the latter is rare in young children.[20]

Reticuloendotheliosis may involve the jaws of children, but the lesions are purely destructive.[21] Foci may be present elsewhere in the skeleton.

Hyperparathyroidism may rarely produce cyst-like expansile lesions in the mandible. It is differentiated by its rarity in young children, biochemical features, asymmetric involvement, and pathognomonic roentgen signs of this condition in the jaws and in the phalanges.[16,21]

True giant cell tumor occurs in an older age group. It is found "extremely rarely in the jawbones."[6] It is not bilaterally symmetric. Central giant cell reparative granuloma usually occurs in the 10 to 25 year age group and most frequently involves the premolar and symphysis region of the mandible,[9,21] unlike the distribution in cherubism.

SUMMARY AND CONCLUSIONS

1. Two cases of cherubism are reported. The roentgenographic and differential diagnostic aspects of this disorder are reviewed. The typical case is a child with bilaterally symmetric multilocular areas of radiolucency in the region of the angle of the mandible, with or without posterior maxillary disease, and without bone disease elsewhere. In such instances, the diagnosis is readily made without resort to biopsy.

2. Cherubism is a hereditary fibro-osseous disease which primarily involves the jaws. It is closely related to fibrous dysplasia, and is probably a hereditary variant of this disease.

3. A new sign, the "hard palate" sign, is described. It is useful in assessing posterior maxillary involvement.

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CRANIOSYNOSTOSIS-SYNDACTYLISM

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ISOLATED craniosynostosis is not a common congenital defect. In conjunction with malformations of the extremities or other somatic anomalies it constitutes an even more rare condition.[11,14] In recent years, certain "head-hand" syndromes have been recognized which often have clinical features in common, yet are genetically and roentgenographically distinct.[29] In the following report a number of cases of craniosynostosis associated with hand and foot deformities, as well as other malformations, are described and differentiated.

ACROCEPHALOSYNDACTYLY

A. TYPE I, APERT'S SYNDROME

The combination of acrocephaly and syndactyly is commonly called Apert's syndrome or ACS, Type I.[1] Although most cases are sporadic, 2 generation transmission has been observed and autosomal dominant inheritance has been postulated.[8] The fundamental gene defect probably results in abnormal development of the ossification centers primarily of the head and extremities.[5,21,26,32] The skull is classically short in the anteroposterior diameter, and the forehead is high, broad and prominent. Because of facial hypoplasia, the cheeks are sunken and the teeth are crowded. A relative prognathism is often apparent. The hands and feet show an extreme degree of syndactyly with soft tissue fusion and synostosis of the middle digits, often to such a degree that the affected hand is likened to a spoon or mitten. A careful roentgenographic examination often reveals other anomalies such as progressive synostosis of the feet with increasing age in the following order: calcaneus to cuboid, lateral cuneiform to third metatarsal, navicular to medial cuneiform and fusion of various phalanges at the interphalangeal joints.[28] In older patients, pseudoarthrosis and phalangeal exostoses are often evident and synostosis of the cervical spine can occur. Most cases are mentally defective and show convolutional atrophy, hydrocephalus and other brain anomalies.[3,27]

CASE I. A.P., a white female was seen at the University of Kansas Medical Center for the first time when she was 3 days old for evaluation of multiple congenital defects. She was the product of a full term normal delivery, the first child of normal parents. There was no family history of similar malformations. Physical examination revealed an alert child with an acrocephalic skull and palpable coronal sutures. True hypertelorism was present along with a mild exophthalmos and a midline posterior cleft palate. All extremities were markedly syndactylous, with the hands having the appearance of a spoon or mitten, although the thumbs were largely spared. There was no apparent visual or neurologic deficit and the remainder of the examination was essentially negative.

Routine laboratory studies were normal. Roentgenographic examination of the skeleton revealed craniosynostosis of the coronal sutures (Fig. 1) and bone fusion of the second, third and fourth fingers and the first and second metatarsals; a wide and short first phalanx of the great toe was also noted.

CASE II. J.C., a 9 year old female, had multiple admissions to the University of Kansas Medical Center for surgical correction of congenital malformations consistent with Apert's syndrome. She had acrocephaly, hypoplastic facial bones (Fig. 2, *A* and *B*) and syndactyly of all 4 extremities (Fig. 2, *C–F*). She was mentally alert and no other abnormalities were detected by the remaining physical examination. The family history was unremarkable.

CASE III. M.P., was first seen at the age of 1½ years for correction of severe syndactyly (Fig. 3, *A*, *B* and *C*). She also had acrocephaly

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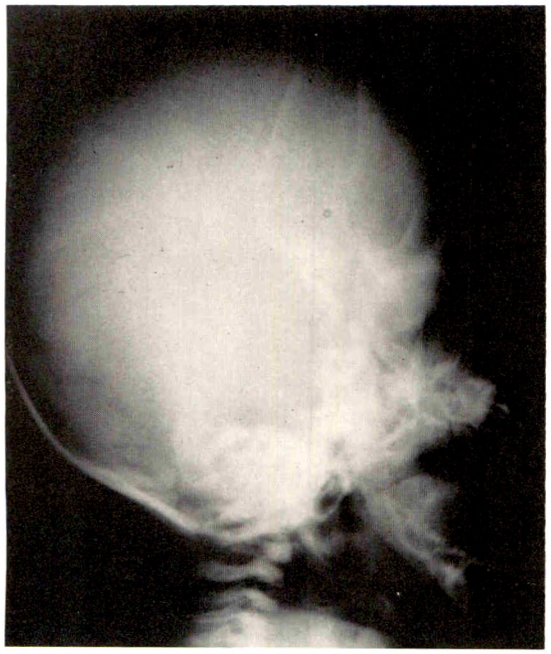


Fig. 1. Case I. Acrocephalic skull due to premature closure of the coronal sutures, hypoplastic facial bones and slight degree of prognatism.

secondary to premature closure of the coronal sutures, hypoplastic facial bones and prominent mandible. No other abnormalities were noted other than mild mental retardation. Her parents and sibs were normal in all respects.

Case IV. M.F., an 18 month old white female, was admitted to this institution for surgical correction of congenital defects and evaluation of mental retardation. She was the offspring of normal parents and the product of a stormy pregnancy that terminated spontaneously 3 weeks prematurely.

Physical and roentgenographic examination revealed a marked degree of acrocephaly with an asymmetric skull, hypoplastic facial bones, gothic palate, exophthalmos and prognathism (Fig. 4, *A* and *B*). She had syndactyly of all 4 extremities along with bilateral equinovarus deformities, spina bifida and pectus excavatum.

A craniotomy was performed but she expired of postoperative complications.

Autopsy revealed pachygyria, hydrocephalus, hypoplasia of the pyramidal tracts, and patent foramen ovale.

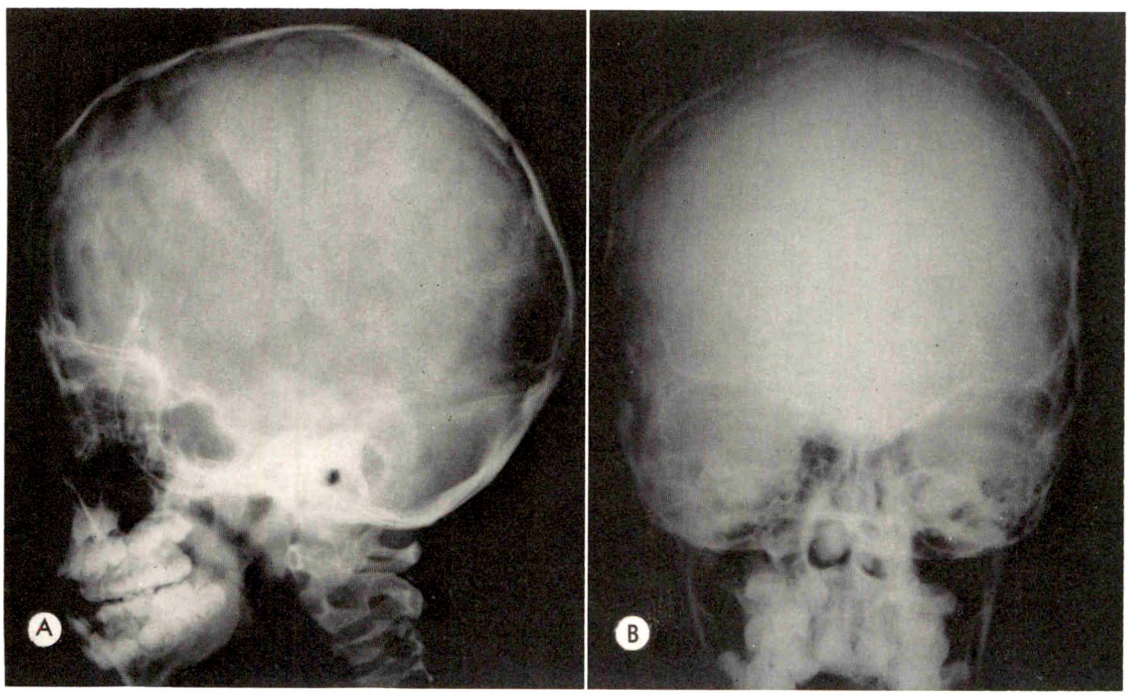


Fig. 2. Case II. A female 9 years of age. (*A*) Lateral view of the skull shows acrocephaly due to synostosis of the coronal sutures (note surgical change) and hypoplastic facial bones. (*B*) Anteroposterior view shows some degree of hypertelorism.

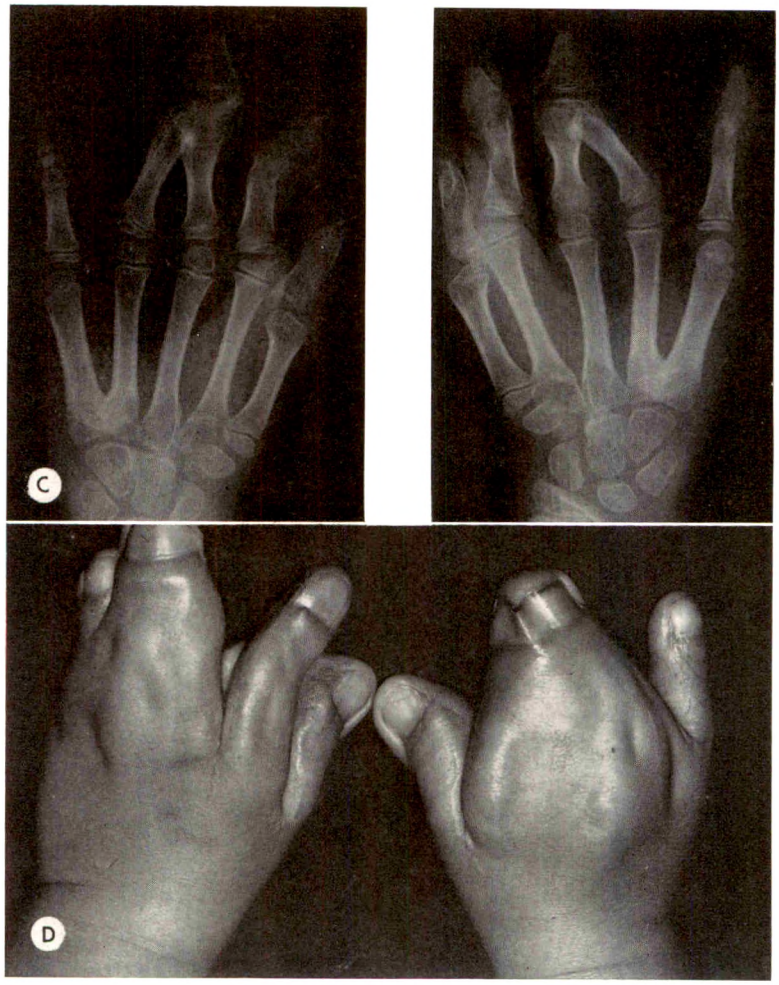


Fig. 2. (*C*) Roentgenographic examination of the hands reveals fusion of the first and second phalanges of all the digits and synostosis at the distal third and fourth fingers with common distal phalanx. (*D*) Marked degree of soft tissue syndactylism.

B. TYPE II, CROUZON'S DISEASE

This type of malformation is known as craniofacial dysostosis or Crouzon's disease.[8,30] Although the combined designation Apert-Crouzon's disease has been used by some workers,[19] extremity changes are minimal or absent even in multiple members of affected families suggesting that Crouzon's disease is a distinct entity. The patient presents with marked degree of acrocephaly, hypoplasia of the facial bones, exophthalmos, hypertelorism and a beaked nose.[9,15,16] However, no definite form can be ascribed to the calvarium as the shape depends on which of the 3 major sutures first becomes synostosed. Visual defects secondary to optic nerve damage may be present and mental deficiency has been described.[22] Study of affected families has established autosomal dominant inheritance for this disorder.

Case v. S.A., a 15 month old white male, was seen in the University of Kansas Medical Center for evaluation of an upper respiratory infection. He was noted to have acrocephaly, hypertelorism, a parrot nose, and low set ears. He had slight bilateral soft tissue syndactyly of the second and third fingers and more prominent webbing between all the toes. Roentgenographic examination revealed craniosynostosis

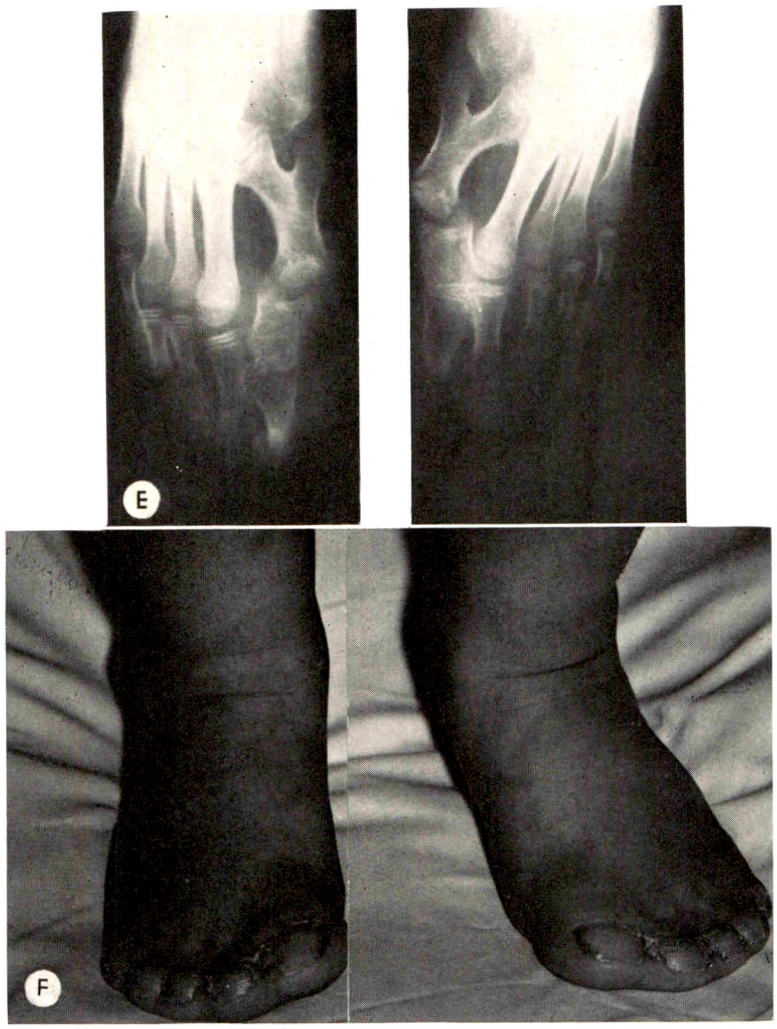


Fig. 2. (*E*) Roentgenographic examination of the feet reveals bifid first metatarsal with partial synostosis with the second metatarsal bone; there is also partial fusion of the interphalangeal joints of the great toes. (*F*) Severe syndactyly involving all the toes.

with acrocephaly, facial hypoplasia and hypertelorism (Fig. 5, *A* and *B*). There was no synostosis of the hands and feet (Fig. 5, *C* and *D*). Other family members were affected with similar malformations (Fig. 6). No mental retardation was evident in any individual.

ACROCEPHALOPOLYSYNDACTYLY

A. TYPE I, CARPENTER'S SYNDROME, NOACK'S SYNDROME

The main features of Carpenter's syndrome are peculiar facies, asymmetry of the skull, polydactyly, brachymesophalangy, mild soft tissue syndactyly, obesity, hypogenitalism and mental retardation. Additional nonspecific abnormalities such as genu valgum, coxa valga, pes varum, abdominal hernias, congenital heart disease, and diabetes mellitus,[4,29,30] may be present.

The skull changes are usually not as severe as in the other syndromes previously discussed.[11,14,25] The polydactyly is preaxial; that is involving the thumbs and great toes, rather than the more common type with extra postaxial digits.[19,29,31] Syndactyly is of the soft tissue type and although brachymesophalangy is present, no bone fusion has been noted.

Of the few reported cases of this syn-

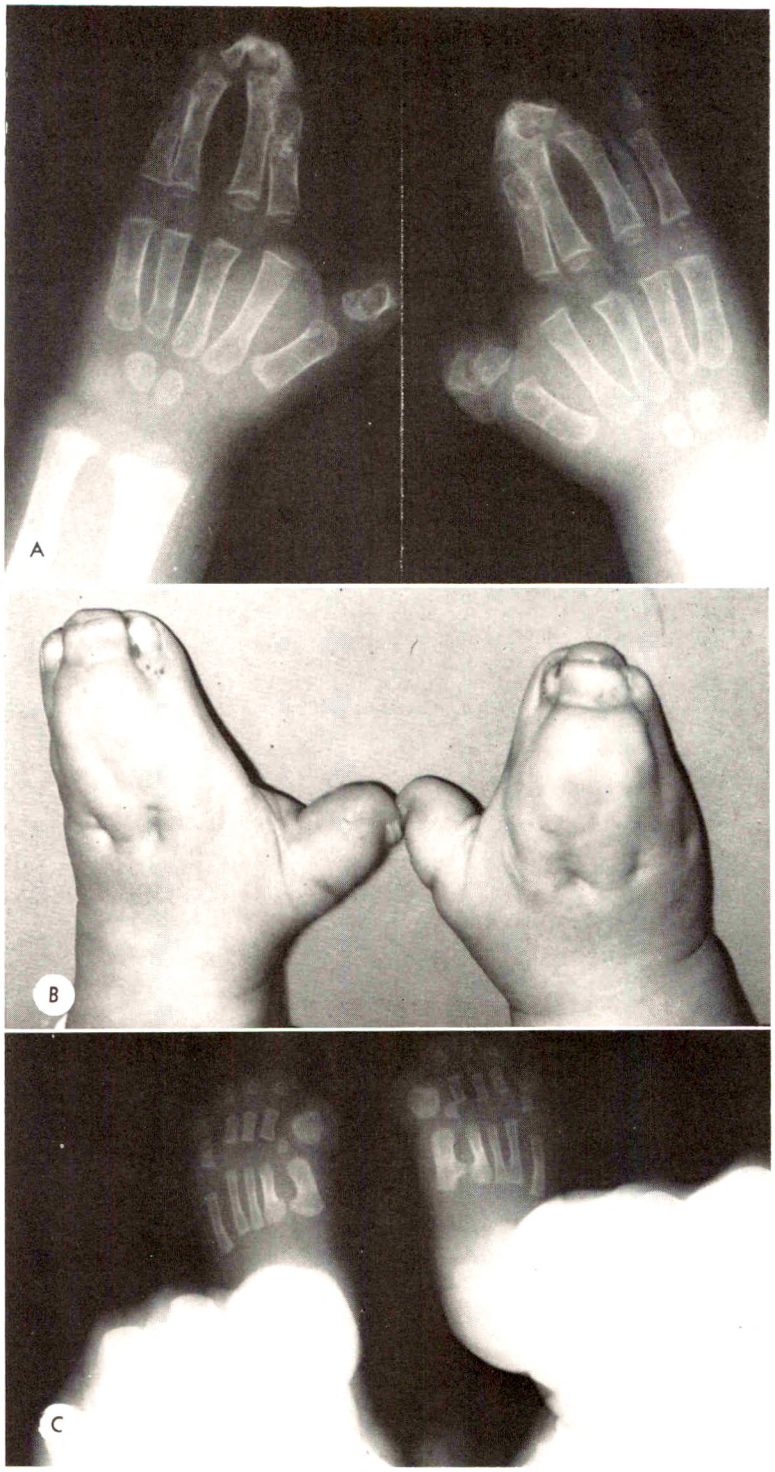


FIG. 3. Case III. A female at 1½ years of age. (*A*) Partial synostosis of the second, third, fourth and fifth digits at the distal portion on the left hand and second, third and fourth on the right, note also fusion of all proximal interphalangeal joints. (*B*) Extensive soft tissue syndactyly of both hands. (*C*) The feet show soft tissue syndactyly, partial synostosis of the first and second metatarsal bones and broad distal phalanx of the great toes.

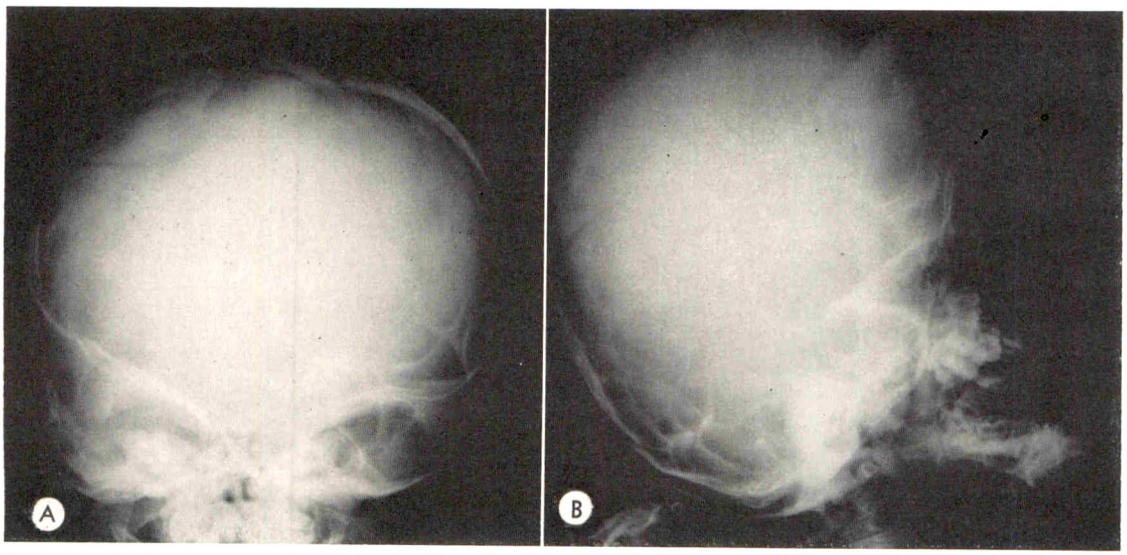


Fig. 4. Case iv. A white female at 18 months of age. (*A*) Anteroposterior view of the skull shows hypertelorism and asymmetry of the frontal area. (*B*) Lateral view shows acrocephaly due to premature closure of the coronal sutures, marked degree of hypoplasia of the facial bones with crowding of the upper teeth and marked degree of prognatism.

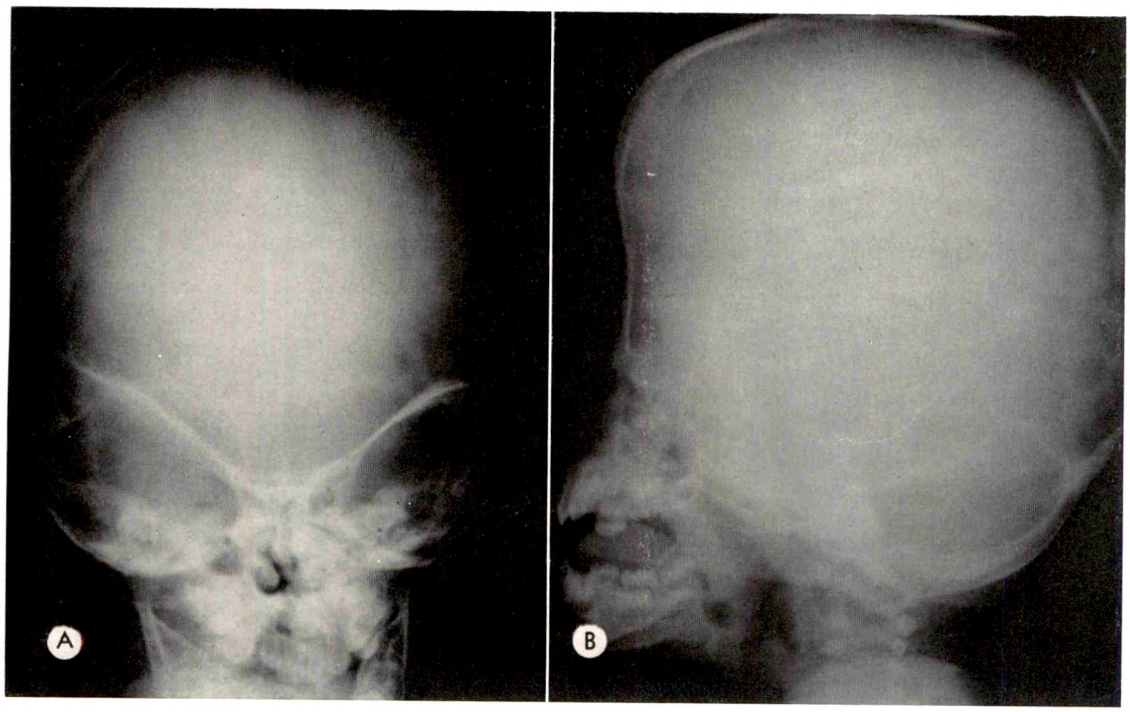


Fig. 5. Case v. S.A. Male at 15 months of age. (*A*) Anteroposterior projection of the skull showing hypertelorism. (*B*) Lateral view shows acrocephaly and hypoplasia of the facial bones.

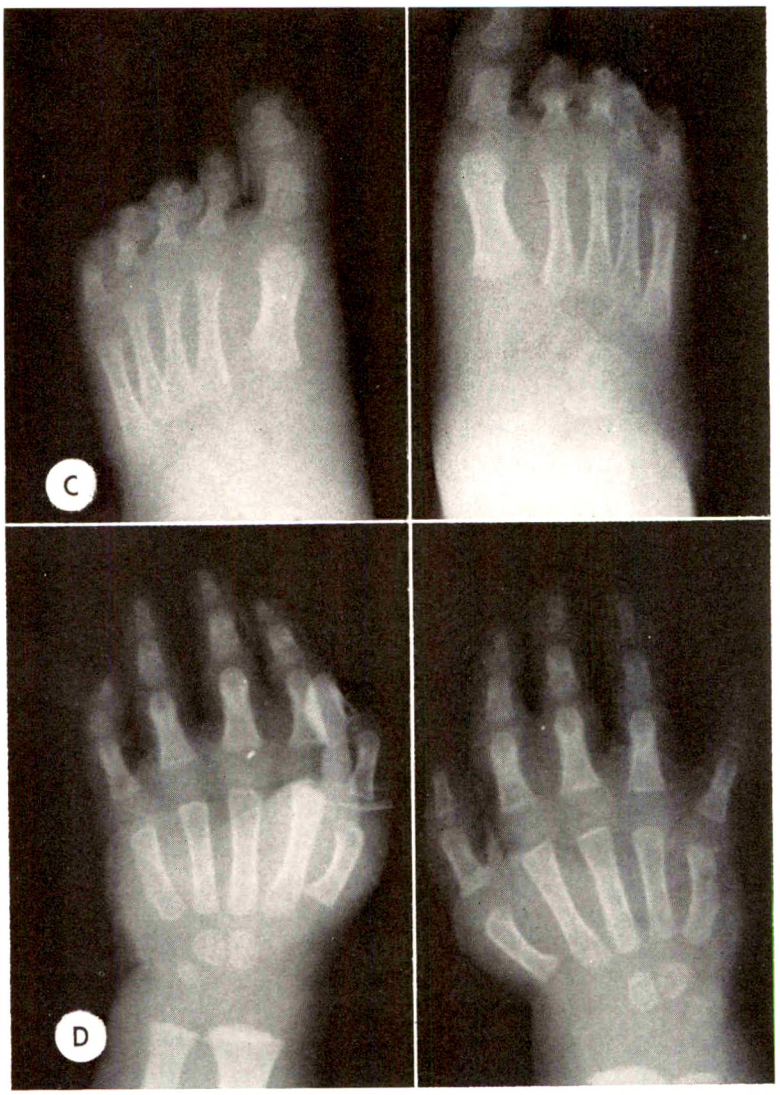


FIG. 5. (*C* and *D*) All the extremities revealed no bone abnormalities but mild soft tissue syndactylism more marked in the feet.

drome, 12 have been familial and 3 sporadic. The occurrence in sibs with unaffected parents suggests autosomal recessive inheritance.[5,10,24,29] However, 2 generation transmission of this symptom complex has been described by Noack[23] and Creig[7] and the possibility that genetic heterogeneity exists cannot be excluded.[19]

CASE VI. B.L., a 45 year old white female, had been followed in the University of Kansas Medical Center for many years. Both parents and 2 sibs were normal and there was no consanguinity. Preaxial polydactyly of the feet had been partially corrected shortly after birth. Early in life she was noted to be mentally retarded and to have diabetes. More recently her menses had become irregular and scanty.

Physical examination revealed a peculiar facies with both dolichocephaly and trigonocephaly. There was no hypertelorism or abnormal nasal configuration. She was obese with a large umbilical hernia and slight webbing of the neck. She had broad short thumbs, clinodactyly of both second and fourth fingers and minimal soft tissue syndactyly. Bilateral genu valgum was present.

Roentgenographically, the skull showed

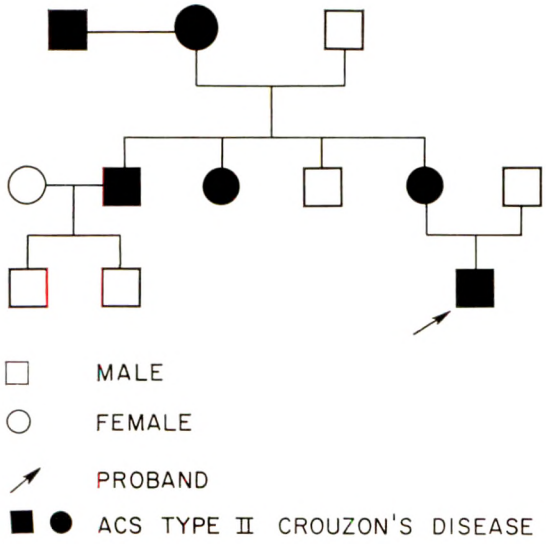


Fig. 6. S.A. (Case v). Kindred.

changes consistent with early closure of the sagittal and metopic sutures (Fig. 7, *A* and *B*). The proximal phalanx of the thumbs appeared to be reduplicated, and there was brachymesophalangy and deformity of the second and fifth digits (Fig. 7, *C* and *D*). The feet showed the residual of preaxial duplication, and a bifid first metatarsal bone on the right. There was also what appeared to be an exostosis on the left first metatarsal bone (Fig. 7, *E* and *F*). Pelvic roentgenograms showed iliac flaring and slight coxa valga. In addition to the genu valgum, degenerative changes were noted in both knees.

Case vii. S.M., a 30 month old white male, was admitted to this institution because of premature closure of the cranial sutures. He was the product of a full term, normal pregnancy. Both parents were normal, and there was no history of similar problems in the family. The child was noted to have difficulty breathing shortly after birth and this was attributed to a large ventral hernia. He was also found to have obvious preaxial polydactyly of the feet and clinodactyly of the second and third fingers in addition to the skull deformity.

Roentgenographic examination showed premature closure of the coronal and metopic sutures. The terminal phalanx of the left great toe was present in duplicate, and the proximal phalanx of the right great toe was also paired. Both first metatarsals were short and broad. The thumbs were broad and appeared to be reduplicated (Fig. 8, *A* and *B*). The second and fifth digits were deformed because of brachymesophalangy and mild soft tissue syndactyly was observed.

B. Type II, Laurence-Moon-Biedl-Bardet Syndrome

This syndrome was first described by Laurence and Moon in 1886.[17] The main

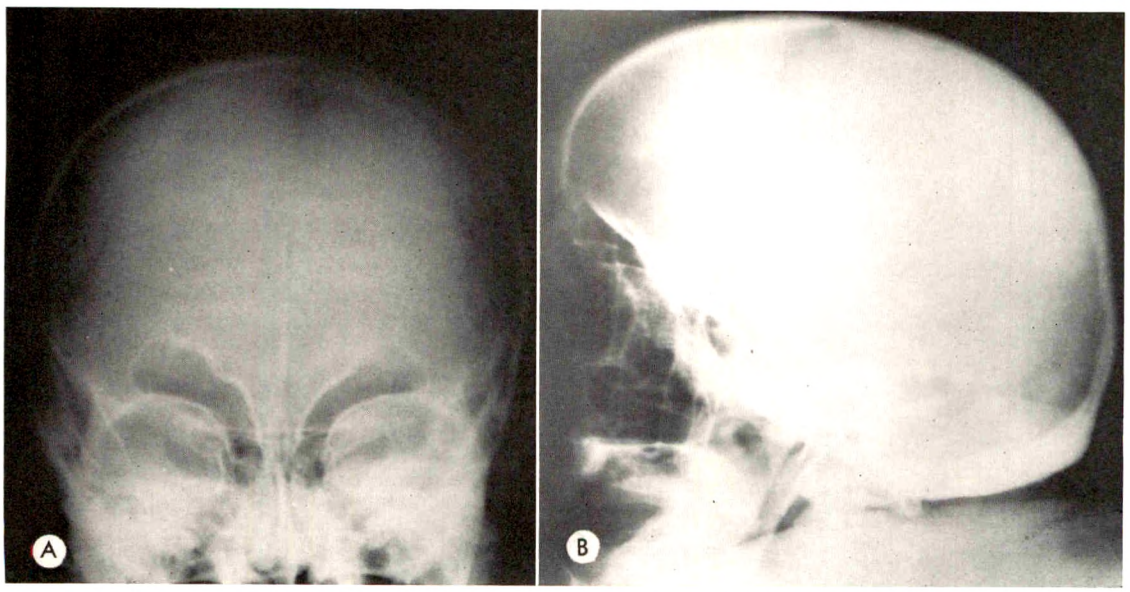


Fig. 7. Case vi. A 45 year old white female. (*A*) Signs of premature closure of the metopic suture producing trigonocephaly. This was more evident clinically. (*B*) Dolichocephaly due to premature closure of the sagittal suture.

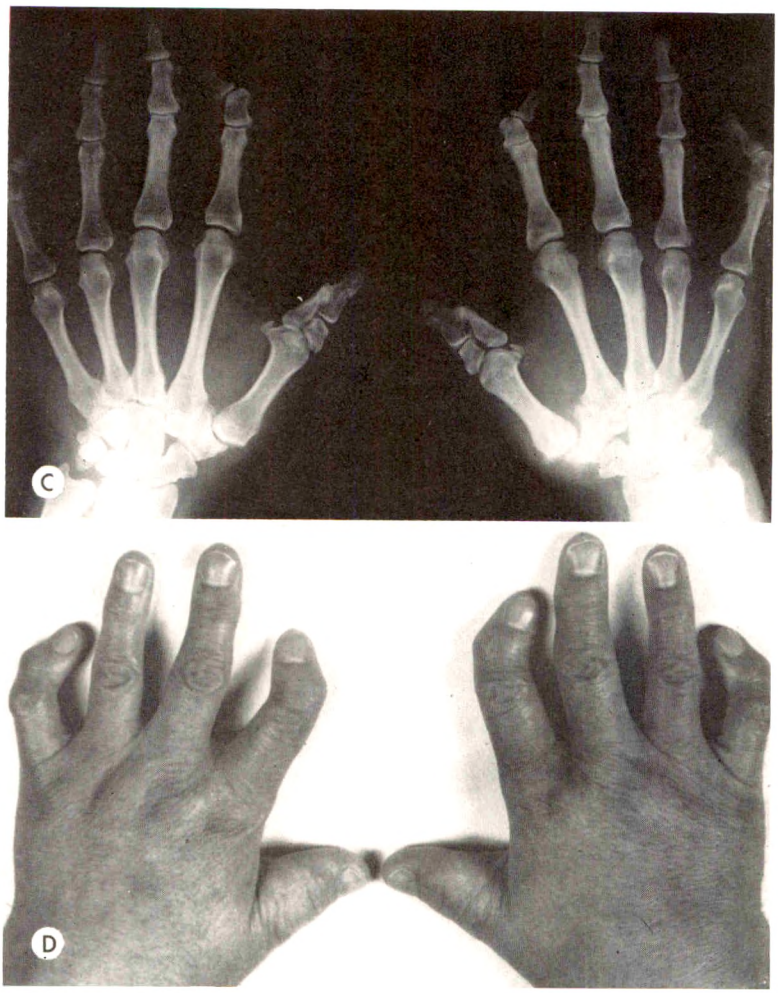


Fig. 7. (*C*) The hands reveal typical changes of Carpenter's syndrome with broad thumbs due to an extra phalanx, deformity of the second and fifth due to brachymesophalangy. (*D*) Minimal soft tissue syndactylism.

clinical features are obesity, hypogonadism, mental retardation, postaxial polydactyly and retinitis pigmentosa.[2,6,12,13] Acrocephaly, dwarfism, deafness, dental anomalies, congenital heart disease, renal malformations, and various endocrine abnormalities may be present.[20] Although many subsequent cases have been reported since the original description, only 20–30 per cent have shown the complete picture. Autosomal recessive inheritance seems established for this disorder, although the presence of such a spectrum of clinical features suggests the possibility that more than a single syndrome may be involved.

Case viii. J.P., a 4 year old white male, was first seen at the Kansas University Medical Center at the age of 2 years for evaluation of poor vision and polydactyly. He was the offspring of normal parents and no similar problem was present elsewhere in the family. No consanguinity was known. He was noted early in life to have an oscillating nystagmus and bilateral retinitis pigmentosa was detected. Postaxial polydactyly of all 4 extremities was noted at birth and the extra fingers were amputated. His head was slightly acrocephalic in type; however, roentgenographic examination showed no gross changes. His development seemed to be normal except for some question concerning his intelligence.

DISCUSSION

All of the syndromes presented here are genetically distinct, yet have phenotypic overlap. This is probably due to the fact that all the defective genes act during a relatively short period of embryologic time. For example, combined differentiation of the head and extremities occurs between the 29th and 35th day of embryogenesis.[29] Furthermore, different hand malformations have their origin at different stages of development—the earlier the disturbance the more severe the deformity. The craniosynostosis and severe hand malformations characteristic of Apert's syndrome are produced by a defective gene acting in a period between the 30th and 32nd day of embryonic development, whereas the mild syndactyly with brachydactyly occurs secondary to another defective gene, operating between the 34th and 35th day of embryonic life.

On the other hand, the impairment of differentiation of the hypothalamus, the retina, and the later phases of segmentation and individualization of the digits char-

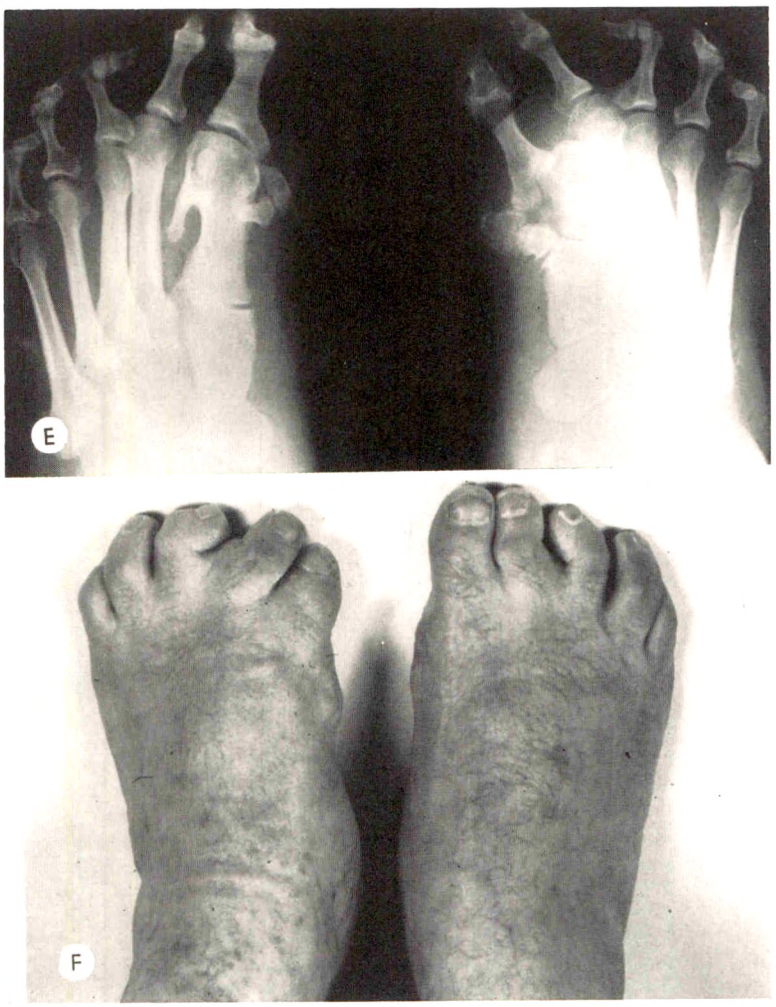


FIG. 7. (*E*) Roentgenographic examination of the feet reveals evidence of previous preaxial polydactyly (partial surgical resection of the extra toes). On the left there is an exostosis at the distal portion of the first metatarsal bone. There is also fusion of the first interphalangeal joint of the second toes and small middle phalanges of the rest of the toes. (*F*) Surgical changes from removal of the extra toes and mild soft tissue syndactylism.

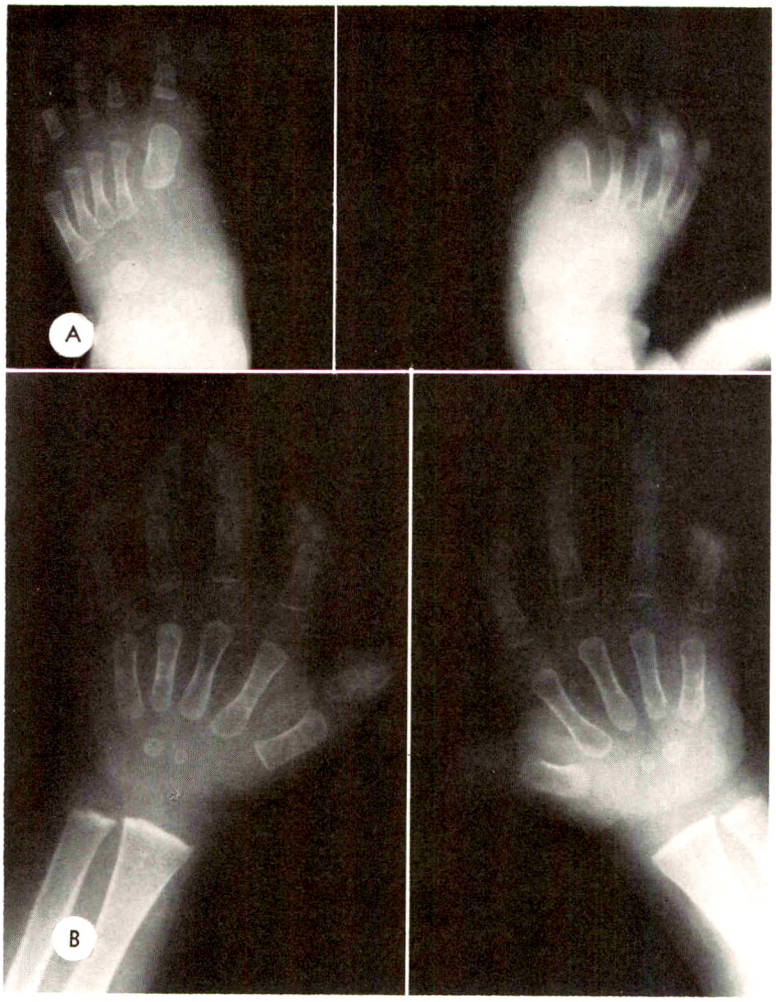


FIG. 8. Case VII. A 2½ month old male. (*A*) The feet show preaxial polydactyly, that is bilaterally extra great toes. The first metatarsal bone is short and broad and there is mild soft tissue syndactylism. (*B*) The hands show broad thumbs due to an extra phalanx, deformity of the second and fifth digits due to brachymesophalangy, and mild soft tissue syndactylism. There was also mild soft tissue syndactylism.

acteristic of the Laurence-Moon-Biedl-Bardet syndrome probably result from still another abnormal gene acting somewhat later, in the period between the 6th and 7th week of intrauterine life. Carpenter's syndrome, which has features in common to both the Apert's syndrome-Crouzon's disease group and to the Laurence-Moon-Biedl-Bardet syndrome, probably results from a genetic abnormality occurring at an intermediate time.

SUMMARY

A number of syndromes with phenotypic overlap involving craniosynostosis, extremity malformations and other somatic defects are reviewed along with illustrative case reports.

All of these entities discussed are hereditary and result from distinct defective genes acting at different, but closely related periods of embryologic development.

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METATROPIC DWARFISM*

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MAROTEAUX and associates[9] have recently separated a clinical entity from the mixed group of short-limbed dwarfs, which they have designated as metatropic dwarfism. Three of our patients with short-limbed dwarfism fall into this category.

REPORT OF CASES

Case 1. Hospital No. 13648. This white male was first seen at Henrietta Egleston Hospital at the age of 16 months and was clinically thought to be an example of spondyloepiphyseal dysplasia. He was noted to have a disproportionately large head measuring 15¾ inches in circumference, a short neck, blue sclerae, a cleft palate, a short sternum, diastasis recti, kyphosis, disproportionately short femurs and humeri, large hands and feet, and knobby knees. He had done fairly well at home and seemed alert and playful to his parents, but had not yet been able to sit unsupported. He could support his head for only a minute or two. Family history and other past history were unremarkable.

Laboratory studies showed a negative urine for chondroitin sulfate. The urine showed moderate amounts of histidine, alanine, glutamine, glycine, taurine, glutamic acid, beta aminoisobutyric acid, and trace amounts of aspartic acid, tyrosine, leucine, and lysine. A small unknown spot was seen on chromatography.

Roentgenographic studies at 3 months of age demonstrated the following:

Skull. Normal with no shortening of the base or frontal bossing.

Cuboid bones. Platyspondyly with a one-third height/anterposterior ratio of the thoracolumbar vertebrae with the exception of a wedged vertebra at L1. No kyphoscoliosis (Fig. 1).

Flat bones. Short and deep sacroiliac notches with squared iliac wings and flat acetabular roofs.

Long tubular bones. Short length associated with swollen metaphyses, especially noted in the proximal femurs at the trochanteric area.

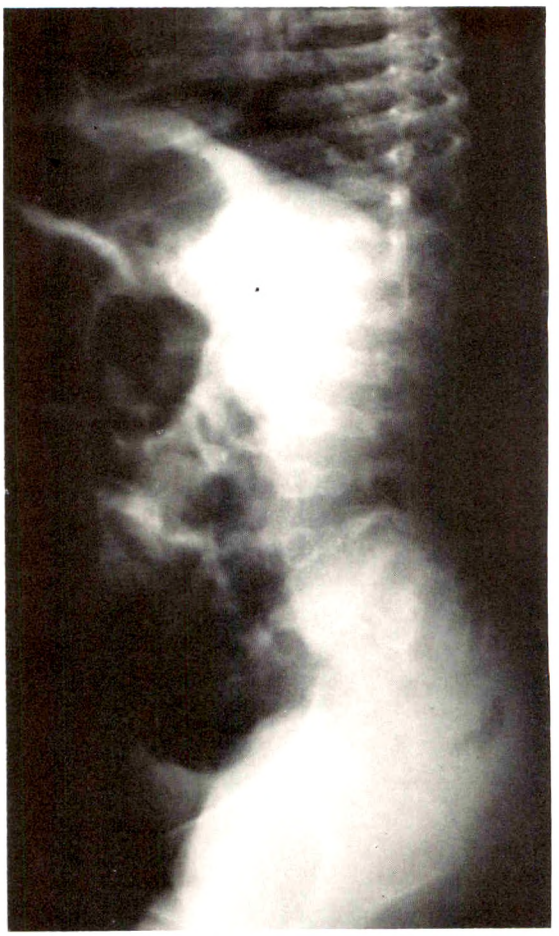


Fig. 1. Case 1. This lateral roentgenogram was taken at the age of 3 months and shows platyspondyly without kyphoscoliosis, a wedged vertebra at L1 and short femurs with flared metaphyses.

Short tubular bones. Not seen on this study.

Roentgenographic studies at 16 months of age revealed the following:

Wrist. For bone age this shows 15 months.

Skull. Remains within normal limits with a normal basal angle.

Cuboid bones. Fragmentation of L1 with slight progression of the platyspondyly. A min-

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imal scoliosis is present. The pedicles are 19 mm. apart at T12, 22 mm. apart at L1 through L4 and 21 mm. apart at L5.

Flat bones. There has been growth without any appreciable change in contour.

Long tubular bones. The physeal-physeal length of the tibia has grown from 5.3 cm. to 7.3 cm. Metaphyseal swelling persists but is not as marked as 13 months ago. Metaphyseal trabeculation is coarse and the metaphyses appear demineralized.

Short tubular bones. The hand phalanges and thumb metacarpal are short and plump.

The patient was lost to follow-up.

Case II. Hospital No. 10843. The only recognized abnormality at the birth of this child was a large hemangioma over the left face and forehead. The patient was adopted at the age of 10 days, and no family history is available. Pyloric stenosis was surgically repaired at the age of 5 weeks. Thoracic scoliosis and the "stigmata of achondroplasia" were first noted at another hospital at the age of 6 months during therapy for a moderately severe respiratory infection.

At 11 months of age she was admitted to Henrietta Egleston Hospital for excision of the ninth through twelfth ribs on the right, including the costo-transverse ligaments. This was followed by casting in an attempt to correct a progressive scoliosis. Only a routine presurgical laboratory work-up was obtained.

Follow-up of the patient showed progressive increase in the scoliosis, despite the surgery and casting.

Roentgenographic studies at 2 months of age revealed the following:

Skull. Not shown.

Cuboid bones. Platyspondyly with one-third height/anteroposterior ratio and stippled irregular ossification. No kyphosis or wedge vertebrae are noted. Mid-thoracic scoliosis measures 35 degrees. The pedicles at L1 and L2 are 14 mm. apart and at L3 through L5 are 15 mm. apart.

Flat bones. Short deep sacroiliac notches, squared-off iliac wings, and flat acetabular roofs.

Long tubular bones. Hyperplastic trochanters. These bones show decrease in length with swollen metaphyses.

Short tubular bones. Not shown.

Roentgenographic studies at 11 months of age demonstrated the following:

Wrist. For bone age this shows no carpal ossification, which corresponds to a newborn.

Skull. Normal.

Cuboid bones. There is rotary scoliosis with 60 degrees of angulation with the main convexity centered at T11. Platyspondyly and stippled irregular ossification persist.

Flat bones. The pelvic configuration is unchanged.

Long tubular bones. The physeal-physeal length of the tibiae has grown from 5.3 cm. to 9.2 cm. Metaphyseal swelling persists.

Short tubular bones. These are within normal limits except for delayed skeletal age (Fig. 2).

Roentgenographic studies at 21 months of age showed that the thorax is long and cylindrical. There has been no appreciable degeneration in the scoliosis since the past examination.

Case III. Hospital No. 18000. This white male was first seen at Henrietta Egleston Hospital at the age of 4 years after he had been treated with leg braces for a pigeon-toed gait with severe bowlegs. No improvement was noted during 1 year of this treatment.

Physical examination showed internal rotation of both lower extremities, apparent flattening of the feet and severe genu varum. There was ligamentous instability of both knees and the medial menisci could be felt to click beneath the finger when the joint was passively manipulated. Bilateral femoral osteotomies were performed but the genu varum continued to progress, and was actually worse $1\frac{3}{4}$ years postoperatively than it was preoperatively.

Roentgenographic studies at 22 months of age demonstrated the following:

General. The thorax is long and cylindrical. The wrist for skeletal age corresponds to the newborn.

Skull. Within normal limits. Basilar angle is 132 degrees.

Cuboid bones. Platyspondyly with a one-third height/anteroposterior ratio and stippled irregular ossification. No kyphoscoliosis. The pedicles at L1 through L3 are 19 mm. apart, at L4 are 20 mm. apart, and at L5 are 25 mm. apart.

Flat bones. Flat acetabular roofs, squaring of the iliac wings and short deep sacroiliac notches.

Long tubular bones. Trumpet-shaped metaphyses and slightly hyperplastic trochanters. The extremities are disproportionately short. A femora vera deformity is noted.

Short tubular bones. These appear plump, possibly because of the delayed bone age and lack

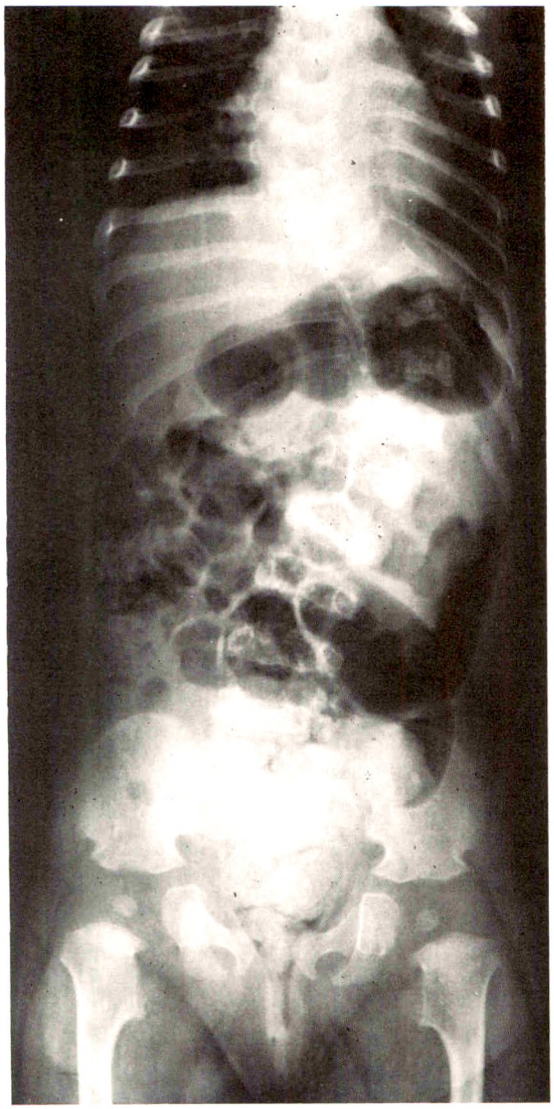


Fig. 2. Case II. This anteroposterior roentgenogram was taken at 11 months of age and shows platyspondyly and rotary scoliosis, a pelvis typical of achondroplastic dwarfism, a cylindrical thorax and swollen lesser femoral trochanters.

of showing of any epiphyses.

Roentgenographic studies at $5\frac{3}{4}$ years of age disclosed the following:

General. There is beginning kyphosis. The wrist for bone age shows 3.5 years. The soft tissues about the knees are dense and excessive, giving him clinical "knobby knees."

Skull. Remains normal.

Cuboid bones. There is progressive platyspondyly associated with upper thoracic kyphosis but no appreciable scoliosis.

Flat bones. The pelvic contour remains unchanged.

Long tubular bones. Bilateral osteotomies have been performed but the bowlegs have continued to progress so that now they are worse than on preoperative studies.

Short tubular bones. The metacarpals and fingers appear normal without evidence of arachnodactyly (Fig. 3; and 4).

DISCUSSION

The classification of short-limbed dwarfism has stimulated considerable speculation over the years. Bullard and George[1] in 1908 recognized two groupings in their article on achondroplasia. The first group was the classical achondroplast, but the second group showed "more definite pathological changes such as scoliosis, kyphosis and lordosis of the spine, coxa vara, genu valgum or varum, and ankylosis, partial or complete of one or more joints, due either to a mechanical inhibition of joint motion or to pathologic changes within the joint." Here they were apparently describing the entity that Maroteaux prefers to call metatropic dwarfism, and what others have called hyperplastic achondroplasia.

In 1966, Maroteaux, Spranger and

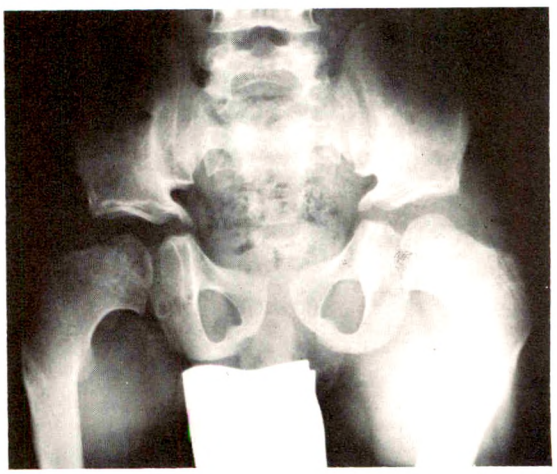


Fig. 3. Case III. This roentgenogram of the pelvis was taken at $5\frac{3}{4}$ years of age and shows the typical horizontal acetabular roofs, short deep sacroiliac notch, square iliac wings and swollen femoral metaphyses. These lesions alone are typical enough to make a tentative roentgenographic diagnosis of metatropic dwarfism.

Wiedemann[9] described metatropic dwarfism, a condition characterized by short-limbed dwarfism and severe kyphoscoliosis. The term "metatropic" means "variable," and was chosen to emphasize the clinical change these patients go through when the spine collapses. One case described by Wheeldon[13] in 1920 in an article on achondroplasia was later described by Pohl[11] in 1939 in an article on Morquio's disease. Clinically, these patients are often confused with other short-limbed dwarf variants at birth. With increasing age there is greater increase in the length of the extremities than would be expected in a classical achondroplastic dwarf. The platyspondyly and kyphoscoliosis then makes these patients resemble spondyloepiphyseal dysplasia in clinical appearance. As yet there are no reported instances of urinary mucopolysaccharides or corneal opacities. In general, these cases have a delayed bone age.

They may be considered to have no clinically recognized abnormalities at birth as Case II in our series. Or, the characteristic roentgenographic findings may be seen as early as 3 months of age, as in our Case I, or at birth.[9] The thorax may be long and cylindrical as in Case III, and views of the pelvis or follow-up roentgenograms of the spine may be needed to differentiate this from asphyxiating thoracic dystrophy.

In contrast to achondroplasia, the skull is always normal. There is no shortening of the base and no frontal bossing. The basal angle between the nasion, sella turcica, and anterior margin of the foramen magnum remains normal.

The vertebral bodies are characterized by platyspondyly, and often have stippled, irregular ossification. Kyphoscoliosis may be seen quite early in life and frequently progresses to a severe degree, despite repeated orthopedic surgery and casting. In contrast to achondroplasia, the lumbar pedicles do not get progressively closer together when they are measured from L1 to L5. A caudal appendage has been described, but this was not seen in any of our cases.

The flat bones of the pelvis are typical of achondroplasia and have flat, horizontal acetabula, short, deep sacroiliac notches and squared iliac wings.

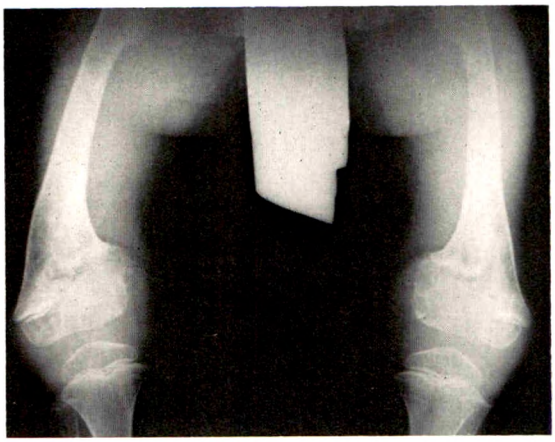


Fig. 4. Case III. This roentgenogram was also taken at $5\frac{3}{4}$ years of age, $1\frac{3}{4}$ years after bilateral femoral osteotomies had corrected a severe genu varum. Metaphyseal flaring is most prominent in the distal femurs. The severe bowing of the legs continued to progress despite orthopedic intervention.

The long tubular bones have trumpet-shaped, expanded metaphyses which are more marked in the femoral trochanters. These bones show an absolute decrease in length initially, but eventually more growth in length is noted than would be expected in achondroplasia. This increase in the length of the extremities accompanied by collapse of the vertebrae and severe kyphoscoliosis produces the classical change in the clinical picture from a short-limbed dwarf with a relatively long thoraco-abdominal axis to a relatively long-limbed individual with a short kyphoscoliotic thoraco-abdominal axis. Case III showed severe genu varum and a pigeon-toed gait which was associated with lax collateral ligaments about the knee. The genu varum became progressively worse despite bilateral femoral osteotomies and postsurgical casting.

The short tubular bones are stubby with irregular borders. Part of this phenomenon is due to the delayed ossification of the epiphyseal centers.

DeGroot[3] described "two atypical cases of chondrodysplasia" in 1951 and had histologic bone studies on his first case which

apparently is a metatropic dwarf. He showed that there was practically absent endochondral ossification in growth cartilage. The trabeculae were very irregular and contained islands of cartilage.

Other distinct entities which fall in the category of short-limbed dwarfism have been identified over the years.[12]

In 1914, Conradi[2] described the first case of dysplasia epiphysealis punctata but believed that he was describing an achondroplastic dwarf. These short-limbed dwarfs have contractures, congenital cataracts and saddle-nose deformity. The micromelia is rhizomelic except for severe involvement in the carpals and tarsals.

In 1934, Jansen[5] described metaphyseal dysostosis as having relatively long upper extremities and bowed, shortened lower extremities. Roentgenographically, the metaphyses were enlarged and irregularly mineralized. Epiphyseal ossification centers were smooth and normal in size or enlarged.

In hypochondroplasia, the affected persons are short-limbed dwarfs, but the disproportion between trunk and extremities is appreciably less than in achondroplasia. This entity may be a mild form of achondroplasia.

In 1940, Ellis and Van Creveld[4] described chondroectodermal dysphasia, a condition of short-limbed dwarfs characterized by polydactyly and ectodermal dysplasia, especially involving the nails and the teeth. The micromelia is acromelic rather than rhysomelic. Congenital heart disease is often associated with this.

In 1955, Jeune and associates[6] ascribed the name thoracic asphyxiating dystrophy to a condition characterized by hypoplasia and shortening of the ribs which result in a narrow, stenotic thorax with limited mobility. The long bones tend to be wide and short but considerable improvement takes place in these as well as in the pelvis with survival. Langer[8] recently emphasized the short extremities and the shortness of the iliac bones in the cephalo-caudal direction. He prefers to call this condition thoracic-pelvic-phalangeal dystrophy, although polydactylia is inconstant and not necessary for the diagnosis.

In 1960, Lamy and Maroteaux[7] coined the term diastrophic dwarfism to describe short-limbed dwarfs with "twisted" extremities and varying degrees of scoliosis. The clubfoot and other torsion anomalies have proved to be very difficult to correct surgically.

In 1965, McKusick *et al.*[10] described the cartilage-hair hypoplasia syndrome which was characterized by dwarfism, metaphyseal irregularity, hypoplasia of cartilage on biopsy and also hypoplasia of hair.

SUMMARY

Maroteaux and associates have recently separated a clinical entity from the mixed group of short-limbed dwarfs, which they have designated as metatropic dwarfism. This disease can usually be recognized at birth, if a sufficient index of suspicion is present.

At birth, the trunk is long and narrow, and the chest is often described as cylindrical. Kyphoscoliosis and platyspondyly are present at this early date, but this is often not noticed clinically. The long tubular bones are short and thickened and have classical hyperplastic proximal metaphyses most noticeable at the lesser femoral trochanters. Bone age is variably delayed. The pelvis shows horizontal acetabula, shortened iliac wings and short, deep sacroiliac notches.

During growth, the tubular long bones lengthen more than would be expected in a true achondroplastic dwarf. The platyspondyly and kyphoscoliosis become progressively worse and the child clinically changes from what at first resembles an achondroplastic dwarf, to what is easily mistaken for spondyloepiphyseal dysplasia. The skeletal deformities usually progress despite orthopedic intervention.

Both the skull base and the interpedicular spaces are normal, which will help in

differentiating this entity from achondroplasia at birth.

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SEQUESTRUM FORMATION IN FIBROUS DYSPLASIA*

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THE roentgen manifestations of fibrous dysplasia are well known and have been repeatedly described in the literature. Therefore, it came as a surprise to encounter a roentgen sign that we could not find previously recorded: sequestrum formation. In each of the 2 patients a sequestrum was seen in the medullary cavity of the tibia within a sclerotic zone of fibrous dysplasia. In neither case was osteomyelitis present clinically or pathologically; in both, the roentgen diagnosis of fibrous dysplasia was confirmed histologically.

REPORT OF CASES

CASE 1. This 7 year old white boy was admitted to the Cincinnati General Hospital in 1956 because of pain in the left lower leg. He had sustained a minor contusion over the middle third of the left tibia a week earlier and had had a very sore throat at that time. He was afebrile, his white blood cell count was 7,000, and the sedimentation rate was normal.

Roentgenograms of the left lower leg showed a large, well-circumscribed area of increased density involving the midportion of the tibia, which was mildly expanded. The cortex and medulla could not be distinguished at the site of involvement. The distal end of the lesion was flame-shaped. Within the proximal medullary portion, a large, square sequestrum framed by a thin radiolucent rim was apparent (Fig. 1, *A* and *B*). Because of the sequestrum, an initial roentgen diagnosis of osteomyelitis was made, but later the diagnosis of fibrous dysplasia was suggested because of the characteristic flame-shaped end of the lesion. Antibiotic therapy was begun. The symptoms remained mild and the roentgen picture unchanged.

At operation 10 days after admission no soft-tissue swelling or periostitis was evident. A window was made in the bone. No pus was seen but a large sequestrum was identified and removed, along with some fibrous material. Fragments of necrotic bone were rongeured from the adjacent walls. Cultures of the specimen were negative. A histologic diagnosis of fibrous dysplasia was made and this was later corroborated by Dr. David C. Dahlin of the Mayo Clinic.



FIG. 1. Case 1. (*A*) Anteroposterior and (*B*) oblique views of the left lower leg. A large sequestrum is seen in an area of fibrous dysplasia. Note the flame-shaped distal end of the lesion and expansion of the tibia.

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A subsequent bone survey revealed an additional lesion in the proximal left femoral metaphysis and diaphysis, typical of fibrous dysplasia (Fig. 2). The patient was asymptomatic when seen 7 months later. Roentgenograms showed no further sequestrum formation (Fig. 3).

Case II. This 12 year old Negro girl was seen in the Emergency Room of the Cincinnati General Hospital in 1967 because of persistent pain in the left leg following a minor injury 2 days earlier. The pain was worse at night but was relieved by aspirin. She was afebrile and had a white blood cell count of 6,000.

Roentgenograms revealed a well-defined sclerotic lesion with tapering of the proximal and distal margins in the midportion of the left tibia (Fig. 4, *A* and *B*). It filled the medullary cavity, narrowed the cortex from within, and slightly expanded the shaft. A bone survey revealed no additional lesions. Laminagraphy 3 days later revealed a large sequestrum surrounded by a thin radiolucent rim in the center of the tibial lesion (Fig. 5). Because of the similarity of the roentgen findings to those in Case I, a diagnosis of fibrous dysplasia with sequestrum formation was made.



Fig. 2. Case I. Anteroposterior view of the proximal left femur shows typical fibrous dysplasia in the metaphysis and proximal diaphysis.



Fig. 3. Case I. Lateral view of the left lower leg 7 months after operation.

At operation 1 week later, laminated subperiosteal new bone was seen overlying the lesion. The cortex was windowed and "dirty-appearing granulation tissue" was encountered. The medullary cavity, filled with sclerotic bone, was curetted. Cultures were negative. Histologically, the sections showed no evidence of inflammation. The final pathologic diagnosis was fibrous dysplasia, concurred in by Dr. Henry L. Jaffe, of New York City.

DISCUSSION

The pathologic nature and derivation of the sequestra in our 2 patients is not known, since in both a curette and rongeur were used and the sites of the individual frag-

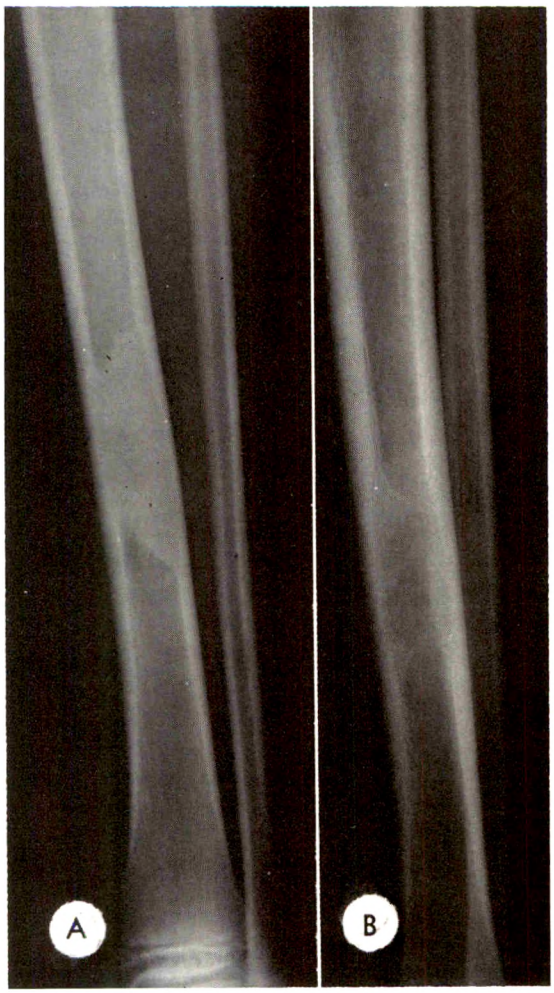


FIG. 4. Case II. (*A*) Anteroposterior and (*B*) lateral views of the left lower leg reveal a sharply defined sclerotic area in the medullary cavity of the left mid-tibia with endocortical thinning.

ments were not identified for the pathologist. However, the absence of clinical, surgical, bacteriologic, and histologic evidence of osteomyelitis excluded infection as a cause.

Benign osteoblastoma and osteoid osteoma were also considered in the differential diagnosis, but the roentgen appearance of the bone surrounding the sequestrum left little doubt that we were dealing with fibrous dysplasia. The flame-shaped lower margin in Case I and the tapering upper and lower margins in Case II, the predominantly medullary location, the relatively osteoblastic character, and the bone expansion are all characteristic of fibrous dysplasia.

Although the duration of symptoms prior to the first roentgenograms was brief in both cases—a matter of a few days—we believe that the sequestra were present for some time, perhaps weeks or months, and that the trauma and consequent pain merely served to draw attention to the condition. The initial roentgenograms in Case II do not show the sequestrum clearly. However, it was probably present at the time and was obscured by inadequate penetration, since it was clearly visible on the laminagrams made only 3 days later.

When observed in the skull, a large sequestrum with a thin radiolucent zone around it has been called a *button sequestrum*. A group of such cases recently reported from this institution[1] included

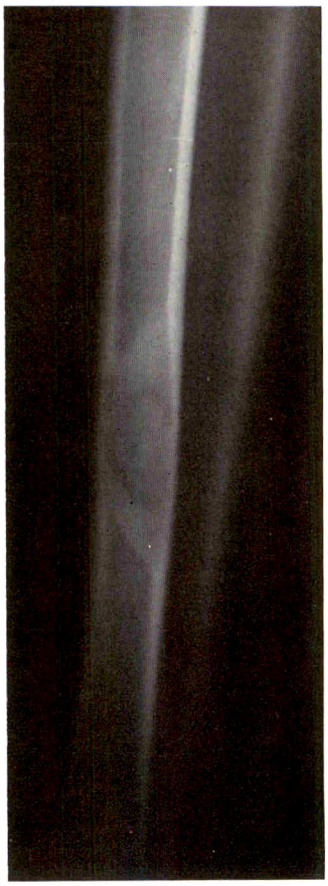


FIG. 5. Case II. Anteroposterior laminagram 3 days later shows a large sequestrum in the center of the medullary lesion.

proved examples of eosinophilic granuloma, tuberculosis, metastatic breast carcinoma, and necrotic bone secondary to radiation therapy for a scalp tumor. Syphilis and osteomyelitis are other causes. The term *button sequestrum* is just as applicable to a long bone lesion of the type described here.

This interesting manifestation, or perhaps complication, of fibrous dysplasia is obviously quite rare. However, failure to recognize the sequestrum on the plain roentgenograms in Case II suggests that some cases are being overlooked. The striking similarity of the 2 cases indicates more than a mere coincidental relationship between the sequestrum formation and the fibrous dysplasia. Familiarity with this roentgen finding may avert a mistaken diagnosis of osteomyelitis and perhaps prevent an unnecessary operation.

SUMMARY

Two cases of fibrous dysplasia of the tibia, each showing roentgenographic evidence of a large sequestrum, are reported. The cause of this rare complication of fibrous dysplasia is unknown. The roentgen appearance is dramatic and diagnostic.

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SPONDYLOTHORACIC DYSPLASIA—A SYNDROME OF CONGENITAL ANOMALIES*

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IN 1966, Lavy, Palmer and Merritt[2] described a new syndrome of congenital anomalies affecting the spine and thorax. The characteristic features of the syndrome consist of a markedly shortened posterior thorax and neck, increased anteroposterior diameter of the chest, protuberant abdomen and severe developmental anomalies of the spine and ribs. They described the condition as occurring in 4 of 7 siblings, the offspring of consanguineous Puerto Rican parents. All 4 affected children died of respiratory infections within the first year of life.

In this report we describe 2 unrelated infants with the syndrome. Both were the offspring of non-consanguineous Puerto Rican parents. Both died from respiratory infection although one lived to the age of 15 months. The characteristic roentgen features are described and illustrated and a descriptive name for the syndrome is suggested.

REPORT OF CASES

CASE 1. E.T. was the third child of non-consanguineous Puerto Rican parents whose 2 other children were normal. The mother had taken 300 mg. of isoniazid hydrochloride daily during her pregnancy because of a positive tuberculin skin test since childhood. Aside from some spotting during the first trimester, the remainder of the pregnancy was uncomplicated. Delivery was unremarkable. Birth weight was 2,300 grams. The infant's appearance at birth was striking in that the neck was short and immobile and the trunk was markedly shortened. There was a prominent thoracolumbar lordosis, and the abdomen was protuberant. The extremities were long and thin, with tapered digits. The vertex-to-heel length was 40.5 cm. Head circumference was 30.5 cm. Chest circumference was 32.5 cm. The remainder of the physical examination was normal.

Roentgenographic examination of the spine and thorax showed extensive and severe developmental anomalies of the cervical, dorsal and lumbar spine. The predominant anomaly was multiple hemivertebrae. There were block vertebrae, and spina bifida was noted throughout the spine, the neural arches being widely open and spread apart. These defects resulted in a marked reduction of the vertical length of the trunk, especially the thorax, and there was a dorsolumbar lordosis which was associated with a protuberant abdomen (Fig. 1, *A* and *B*). The rib-vertebral joints were closely approximated and there was incomplete segmentation of numerous ribs at their posterior extremities. Approximation of the rib-vertebrae articulations in the shortened dorsal spine resulted in a fan-like radiation of the ribs. Skeletal survey showed no other osseous abnormalities.

In spite of her severe chest deformity, the child did well during the first 6 months of life, gaining weight and thriving. During the second 6 months of life, however, she became progressively more tachypneic as a result of her limited ventilatory exchange. She was noted to tire easily with feeding and to be particularly susceptible to upper respiratory infections. Weight gain was poor. In spite of her physical impairment, she was notably alert and active.

At 1 year of age the child weighed 4,000 grams. On the Gesell Developmental Scale, she demonstrated a general maturity level of 56 weeks, with gross motor behavior scattering from 27 to 52 weeks, being severely limited by her skeletal deformities and marked debilitation. Karyotyping of peripheral blood leukocytes revealed normal number and morphology of chromosomes with an XX pattern.

Hospitalizations were necessary at 12 and 14 months of age for pneumonia. In both instances, the child responded rapidly to antibiotic therapy and supportive care. Her third hospitalization was at 15 months of age when she presented in severe respiratory distress from pneumonia. The course of the lung infection was unresponsive to intensive supportive and antibiotic

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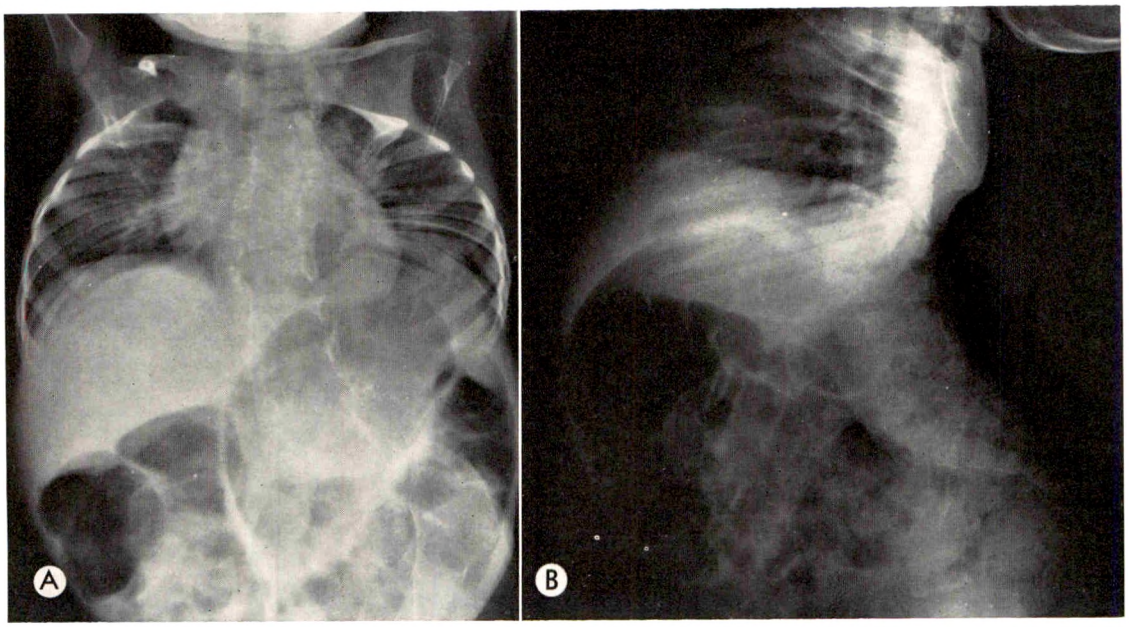


Fig. 1. Case I. (*A*) Anteroposterior projection shows fan-like radiation of the ribs. There is incomplete segmentation of some of the ribs posteriorly. Multiple hemivertebrae and open neural arches are noted with vertical shortening of the thorax and spine. (*B*) Lateral projection shows dorsolumbar lordosis with protuberant abdomen and developmental abnormalities of the vertebrae.

therapy and rapidly resulted in the infant's demise. At the time of this last hospitalization, the child's vertex-to-heel length was 54 cm., and the vertex-to-rump length was 35 cm. Head circumference was 42 cm. Chest circumference was 35 cm.

Case II. W.L. was the fourth child born to non-consanguineous Puerto Rican parents with 3 normal offspring. The pregnancy was uncomplicated, and the child was delivered at term. There was some fetal distress during the delivery and meconium staining of the amniotic fluid was noted at the time of delivery. Birth weight was 2,800 grams. The appearance of the infant was most unusual: The trunk was very short with a marked thoracolumbar lordosis. The abdomen was protuberant. A short and immobile neck gave the head the appearance of rising from the shoulders. The vertex-to-heel length was 41 cm., and the vertex-to-rump length was 22 cm. Head circumference was 32.5 cm. Chest circumference was 33 cm. With the exception of an absent anal reflex and decreased anal sphincter tone, the remainder of the physical examination was unremarkable.

Roentgenographic examination of the spine and thorax showed multiple hemivertebrae, block vertebrae, absent vertebral bodies and diffuse spina bifida with widely spread neural arches. The entire spine was involved by developmental defects. Only 2 sacral segments were present and these were also defective. There was a marked reduction in the vertical length of the trunk, especially the thorax and a dorsolumbar lordosis was associated with protuberance of the abdomen. The rib-vertebrae articulations were closely approximated and there were multiple incomplete segmentations of the ribs which radiated fan-like from the dorsal spine (Fig. 2, *A* and *B*). Skeletal survey showed no other osseous abnormalities. An intravenous urogram showed no abnormalities of the urinary tracts.

The child was discharged at 10 days of age, in no distress and weighing 2,790 grams. He was seen for follow-up examination at 3 weeks of age and appeared to be thriving. He did appear to tire with feeding, however, and peripheral cyanosis was noted when he cried.

The infant was next seen at 1 month of age when he presented to hospital in severe respiratory distress. There was clinical and roentgenographic evidence of bilateral bronchopneumonia. Antibiotic therapy and intensive supportive measures failed to abate the course of

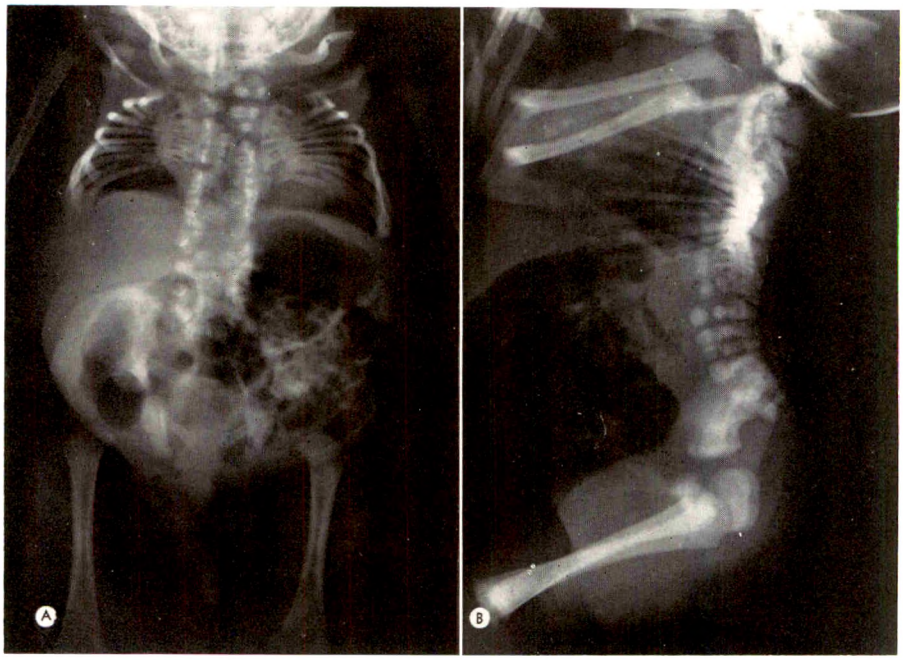


FIG. 2. Case II. (*A*) Anteroposterior projection shows characteristic fan-like radiation of ribs with incomplete segmentation. There are multiple hemivertebrae, absent vertebrae, cleft vertebrae and wide open neural arches. The trunk and neck are shortened in their vertical lengths. (*B*) Lateral projection shows a dorsolumbar lordosis with protuberant abdomen. There are multiple vertebral anomalies including block vertebrae and incomplete ossification of the sacrum.

the lung infection, and the infant was pronounced dead 6 hours after admission.

DISCUSSION

The clinical and roentgen features of this syndrome, as demonstrated in the 6 cases reported to date, are remarkably constant and are sufficiently bizarre to permit easy recognition. There is a markedly shortened posterior thorax. The neck is short and immobile, the head appearing to rise from the shoulders. The abdomen is protuberant in association with a wide sweeping dorsolumbar lordosis. The extremities are long and thin with tapered digits which have an arachnodactylous appearance. The severe developmental anomalies of the spine are responsible for the shortened neck and posterior thorax and are intimately related to segmentation deformities and close approximation of the posterior ribs. The predominant vertebral anomaly is the presence of hemivertebrae. The neural arches are widely open throughout the spine. Some vertebral bodies may be missing altogether and occasional block vertebrae may be noted (Fig. 1, *A* and *B*; and 2, *A* and *B*). The rib-vertebral articulations are always closely approximated so that the ribs radiate posteroanteriorly in a fan-like fashion which is characteristic and readily noted on the roentgenogram. Under any circumstances, multiple thoracic hemivertebrae are almost always associated with segmentation deformities of the ribs—an observation already commented upon by Caffey.[1] In none of the cases so far reported has there been anomalous development of any portion of the skeleton other than the spine and ribs.

All 6 infants died early in life from respiratory infections possibly related to the thoracic deformity and limited respiratory function. The known association of hemivertebrae with pulmonary hypoplasia and agenesis, however, raises the question of whether or not the respiratory disorders in these patients may be related primarily

to abnormal lung development. Resolution of this question awaits definitive pathologic study of the lungs of patients dying with this syndrome. Infantile thoracic dystrophy is another instance in which abnormal thoracic development is associated with frequent early death from respiratory infection.

It appears that this syndrome in infants may be one end of a spectrum of anomalies of spine which ranges from severe and lethal deformity to a milder, non-lethal involvement. Caffey,[1] for instance, has described 2 dwarfed siblings, 8 and 10 years old, with multiple hemivertebrae and segmentation defects of the ribs. The vertebral anomalies extended throughout the entire spine and all bones other than the spine and ribs were roentgenographically normal. The vertebral anomalies were much milder than those described in the infants with this lethal syndrome. The children were dwarfed due to shortening of the neck and trunk. The extremities were normal but appeared relatively long.

Since the developmental abnormalities are limited to the spine and thorax, the syndrome may be described simply as spondylothoracic dysplasia. As there is still no generally accepted definition of the term dysplasia, aside from the fact that it implies faulty development, this designation would seem useful, at least until the classification of disturbances of skeletal growth is further refined.

SUMMARY

Two additional cases of a newly described syndrome of skeletal anomalies are reported and the roentgen features of the syndrome are reviewed.

As the osseous abnormalities are developmental defects and are limited to the spine and thorax, it is suggested that the syndrome be referred to as spondylothoracic dysplasia.

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MULTIPLE EPIPHYSEAL DYSPLASIA*

A CONTRIBUTION TO THE PROBLEM OF SPINAL INVOLVEMENT

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ALTHOUGH multiple epiphyseal dysplasia (MED) has been a well recognized entity since Fairbank's naming and description of the disease in 1946 and 1947,[2,3] no unanimity of opinion has evolved concerning the occurrence of spinal involvement in this disease. There is some question that the spinal changes described in certain reports may be coincidental and not a part of MED. The purpose of this report is to describe a family with rather marked MED but without any evidence of spinal involvement, and to document the variability of the spinal manifestations of this disease.

REVIEW OF THE LITERATURE

Probably the earliest report of MED is that of Barrington-Ward in 1912,[1] in which he described peripheral joint involvement in a brother and sister. Following Fairbank's excellent description of the syndrome, Jackson *et al.*,[7] in 1954, presented a report in which they described vertebral changes in patients who otherwise filled all of the recognized criteria of the syndrome of MED. In that study they noted that "gross localized spinal deformity" in this syndrome had previously been unreported. Since then numerous cases of spinal involvement have been recognized.[4,5,9,11] Generally, the spinal changes reported have been similar to those of Scheuermann's disease with irregularities of the anterior superior and inferior borders, anterior rounding or wedging of the vertebra,[12] and, often, kyphosis. Scoliosis has also been reported. Kozlowski and Lipska[8] referred to a family study of 4 generations with 9 affected members, in which only 1 was found to have spinal changes. Hunt *et al.*[6] recently reported 2 cases of MED in brothers who had spinal changes described as platyspondyly, and in their report, it is stated that all of the cases of MED seen by them have had spinal changes. There is, however, some reasonable doubt that their 2 cases represent true examples of the Fairbank type of MED. It should be noted that there is much variation in the incidence of vertebral involvement in various families with MED. Lamy and Maroteaux[9] found vertebral changes in about two-thirds of the cases in which a roentgen study of the spine was undertaken. Maudsley[11] found vertebral involvement in members of 2 of the 3 families he studied, with 100 per cent involvement in 1 family. It is apparent that the frequency of spinal involvement in this disease has been shown to vary from 100 per cent in some families to total lack of involvement in others. We believe that the lack of spinal involvement in the family presented here is of importance, since it is generally stated that severe peripheral involvement is usually accompanied by involvement of the spine.[10]

REPORT OF CASES

CASE 1. T. G., the propositus, is a 10 year old white female, who was admitted to the University of Virginia Hospital for evaluation of severe pain in both hips on ambulation. The history revealed that at age 22 months, she had had "turning in" of her left foot and had a very unsteady gait. She had been treated in plaster, then braces, for 2 years, but her gait was never normal. At age 5 she was struck by an automobile and sustained fractures of both legs and one wrist. At age 7 she noted the onset of severe joint pain in her lower extremities and was not allowed to bear weight for 1½ years. One month prior to this admission she was hospitalized at her local hospital for severe hip pain. The family history revealed a number of relatives with similar histories (Fig. 1).

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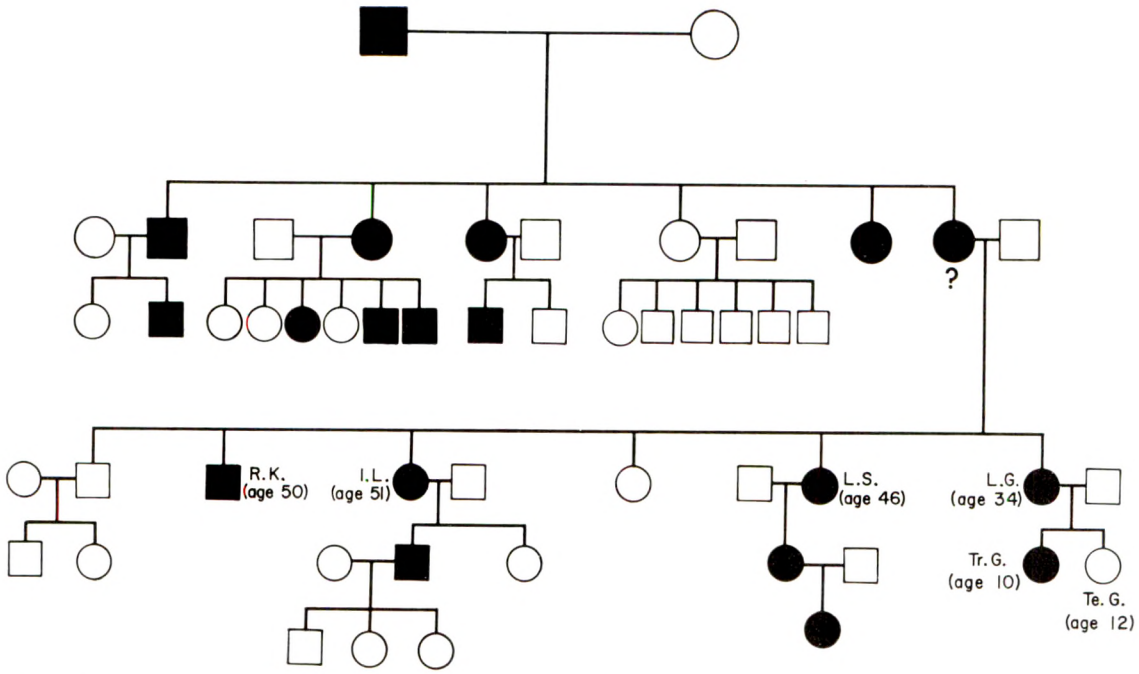


Fig. 1. Case 1. Genealogy. The affected individuals are shown in black. The transmission is typical of an autosomal dominant mode of inheritance, with high penetrance. (?) = Probably affected, data incomplete.

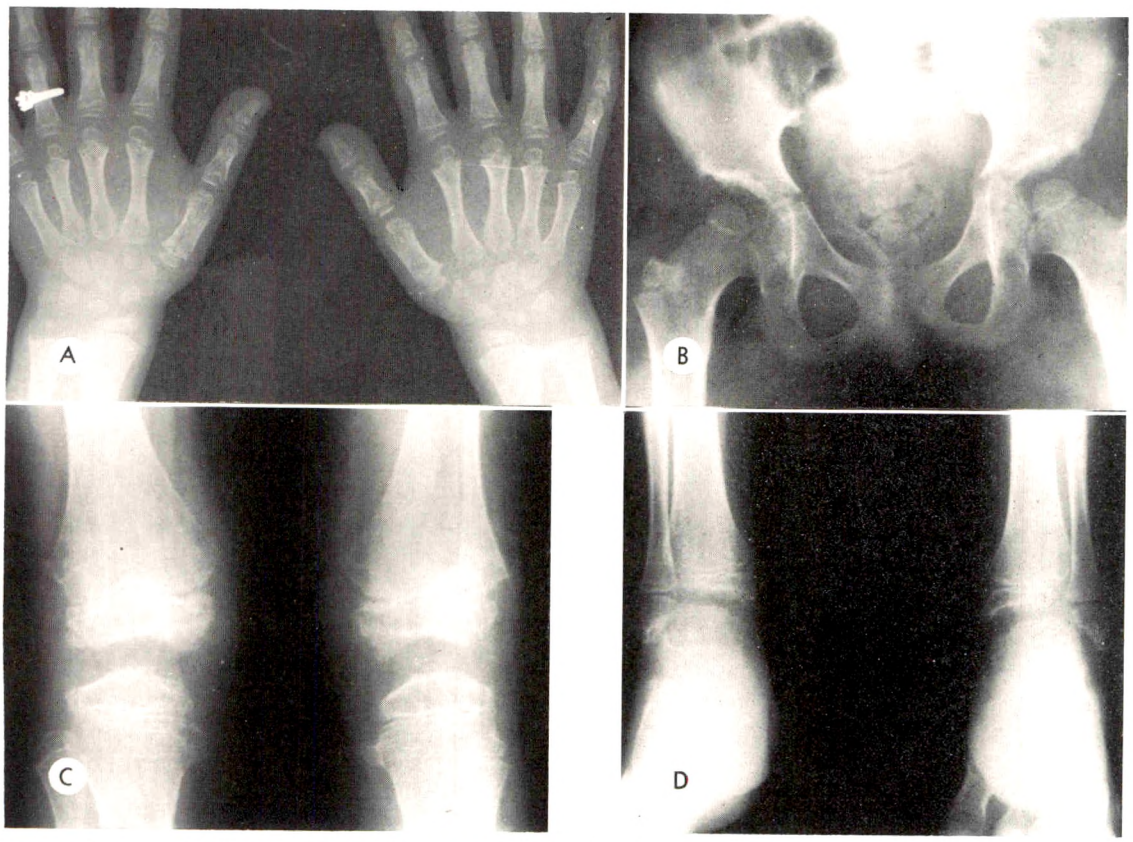


Fig. 2. Case 1. (*A–D*) There is irregularity of epiphyses in all joints, most marked in the wrists and knees.

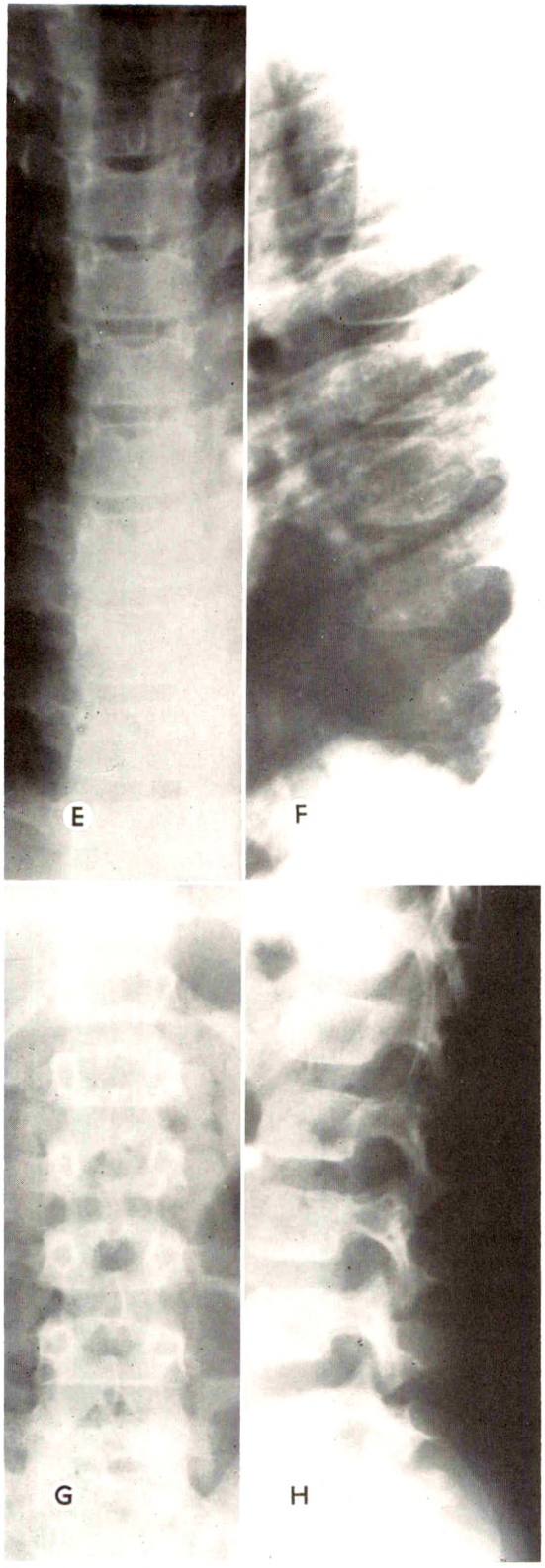


FIG. 2. (*E–H*) There are no spinal changes.

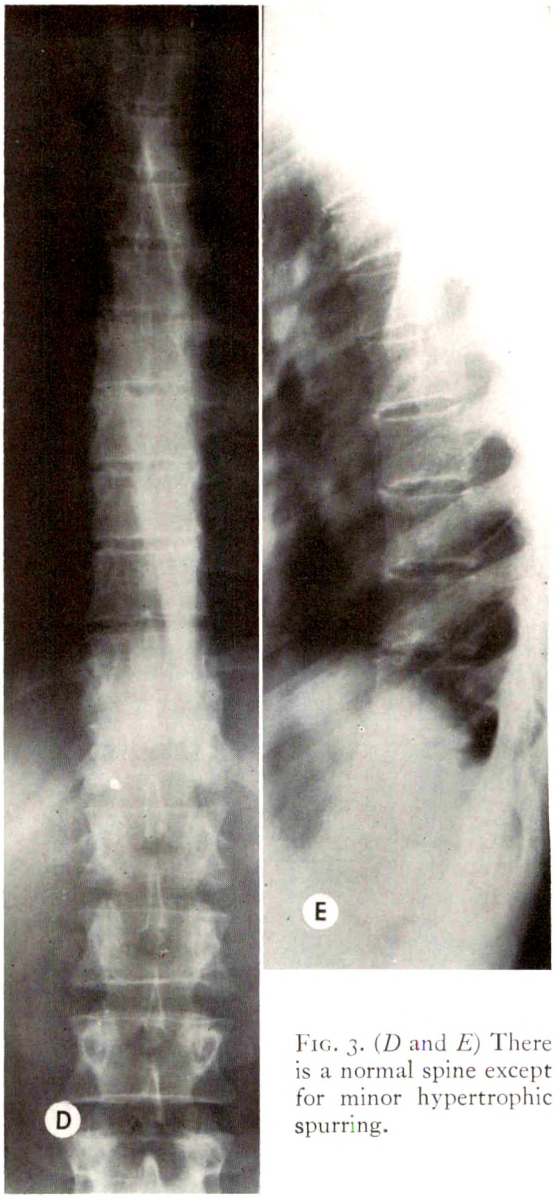


FIG. 3. (*D* and *E*) There is a normal spine except for minor hypertrophic spurring.

Physical examination revealed a diminutive white female child who was alert and intelligent with normal features but short extremities. The upper extremities had normal range of motion but there was bilateral brachydactyly. Motion of either hip was markedly limited by severe pain. The lower extremities were held in adduction, internal rotation and slight flexion, and she could not tolerate weight-bearing on either foot. Neurologic examination was entirely negative and all laboratory studies were within normal limits. Roentgen examination of the hips, knees, ankles, hands and wrists

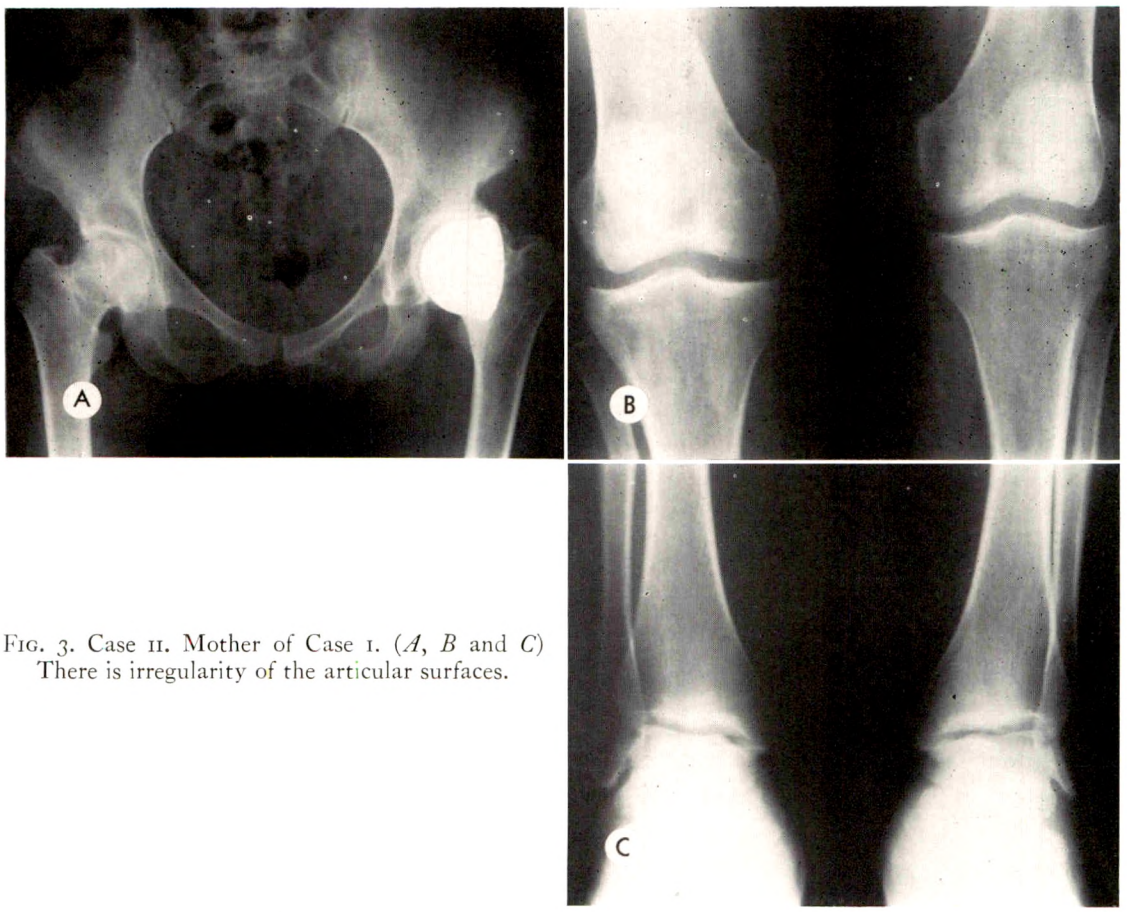


Fig. 3. Case II. Mother of Case I. (*A*, *B* and *C*) There is irregularity of the articular surfaces.

(Fig. 2, *A–D*) showed irregularity of all epiphyseal centers, and of adjacent metaphyses, most marked in the wrists and knees. The acetabular roofs are steep and irregular and the capital femoral epiphysis underdeveloped, as are those of the wrists. Cone epiphyses are seen in the thumbs. There is steep aclivity of the distal articular surfaces of the tibias. Roentgenograms of the spine (Fig. 2, *E–H*) show no abnormalities.

Case II. L. G., age 34, is the mother of Case I. Her height was much below average. She had a history of having had a cup arthroplasty on her left hip, 10 to 12 years before because of "arthritis." Roentgen examination revealed a metallic cup in the left hip with irregularity of the articular surfaces of the right hip, a short femoral neck, irregularity of the articular surface of the knees, steep aclivity and irregularity of the distal tibial articular surfaces (Fig. 3, *A*, *B* and *C*). Roentgenograms of the spine were normal (Fig. 3, *D* and *E*).

Case III. L. S., age 46, is the sister of Case II. She had an average build, was over 5 feet in height. She was completely asymptomatic and had no knowledge of any familial defects. Roentgen examination showed coxa vara deformities with slight irregularity in the femoral heads and irregularity of the articular surfaces of the knees (Fig. 4, *A* and *B*). The ankles show slight aclivity of the articular surfaces of the tali (Fig. 4*C*). The spine is normal (Fig. 4, *D* and *E*).

Case IV. I. L., age 51, is a sister of Case II. She had minor joint complaints. Roentgen examination showed marked degenerative changes in the hips, irregularity of articular surfaces of the knees, and increased aclivity of the distal articular surfaces of the tibias (Fig. 5, *A*, *B* and *C*). The spine shows some minor end plate irregularity in the lower dorsal region (Fig. 5, *D* and *E*).

Case V. R. K., age 50, is a brother of Case

II. He has a history of prosthetic replacement of a femoral head 10 years ago for "arthritis." He uses canes for ambulation and is below average height. Roentgen examination showed a hip prosthesis on the right and degenerative arthritis of the left hip (Fig. 6*A*). The articular surfaces of the knees are irregular and there is marked aclivity of the distal articular surfaces of the tibias (Fig. 6, *B* and *C*). The spine is not remarkable except for evidence of an old compression fracture of the mid-dorsal region (Fig. 6, *D* and *E*).

DISCUSSION

It is apparent from the family study presented here that spinal involvement is not necessarily a consistent feature in MED. Furthermore, the opinion that spinal involvement is a constant feature in individuals with severe peripheral involvement is also not substantiated, particularly in light of the rather severe joint involvement of several of the members of this family.

The literature on this subject indicates that spinal involvement, when present, is the well recognized process of osteochondrosis, and it would appear that this occurs in individuals with MED with greater frequency than one would anticipate in the general population, but there is no statistical proof of this fact. It is, therefore, impossible to be certain whether such involvement is coincidental or follows the generalized skeletal disease.

The family reported here also indicates an interesting consistency in the areas of severest involvement and in the manifestations presented. This is particularly evident in the remarkable similarity in appearance of the knees, and the aclivity of the ankle joints. The variability in severity of in-

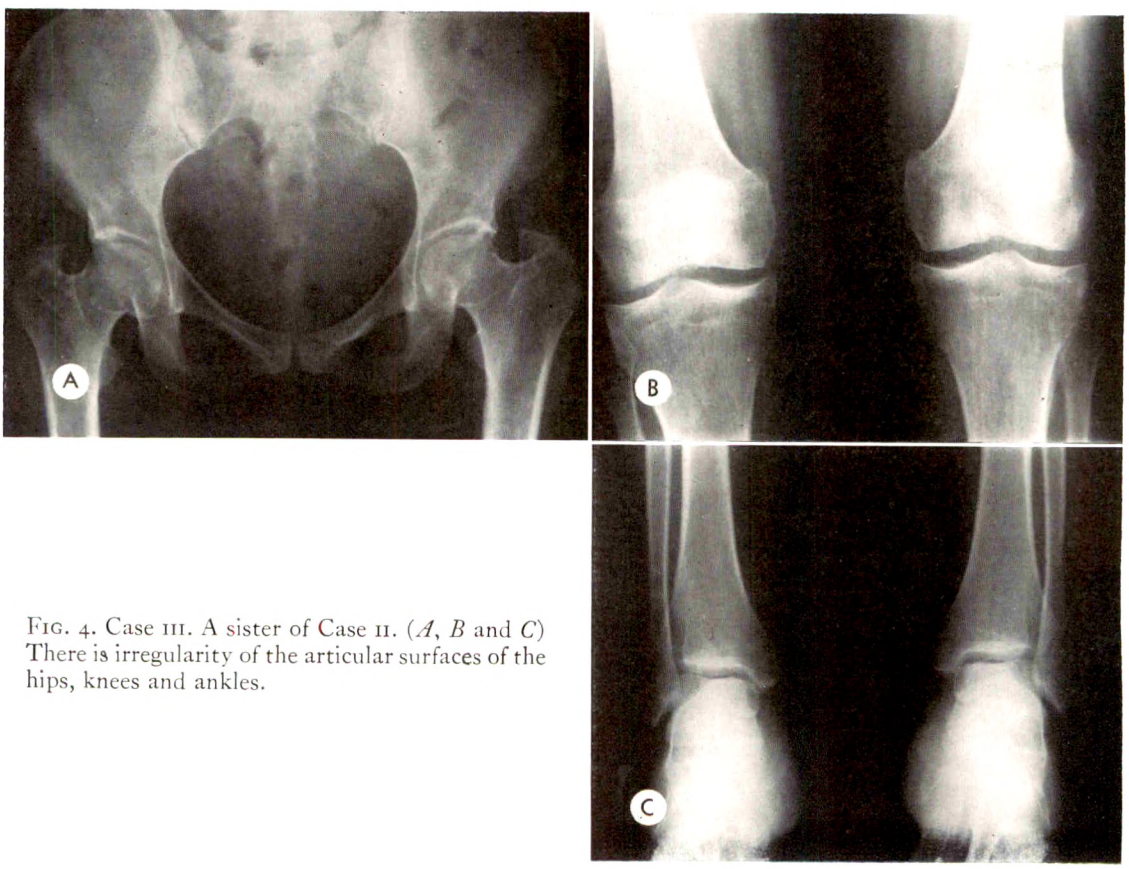


FIG. 4. Case III. A sister of Case II. (*A*, *B* and *C*) There is irregularity of the articular surfaces of the hips, knees and ankles.

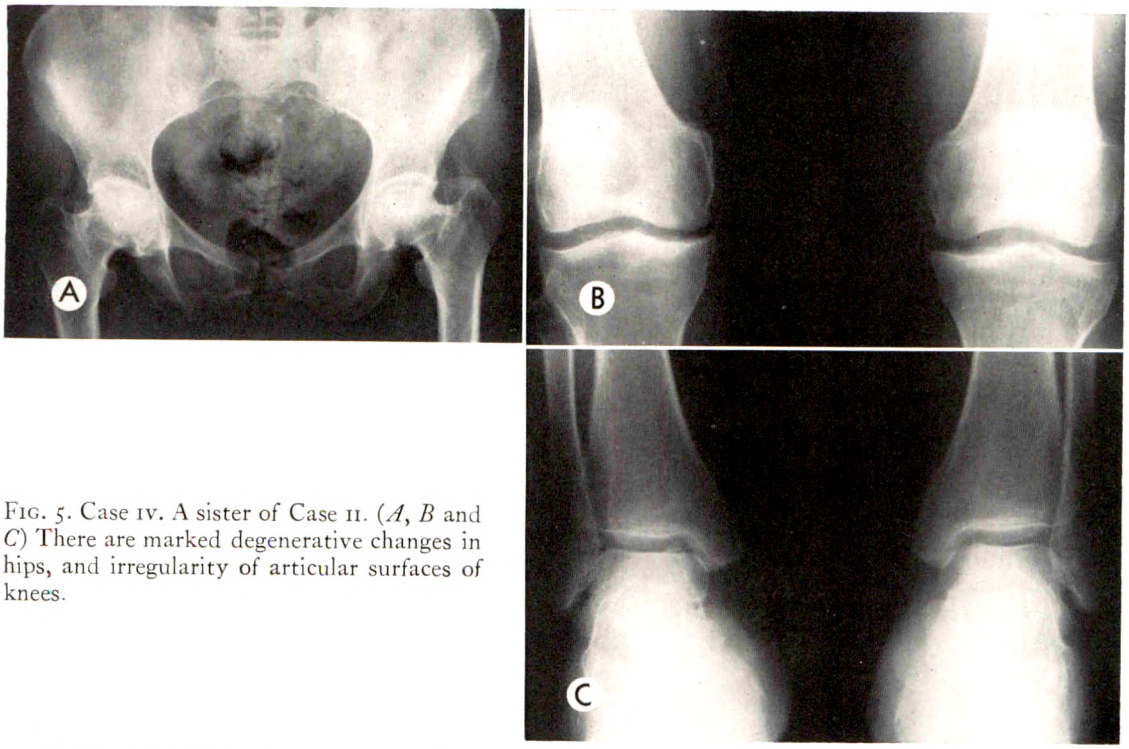


FIG. 5. Case IV. A sister of Case II. (*A*, *B* and *C*) There are marked degenerative changes in hips, and irregularity of articular surfaces of knees.

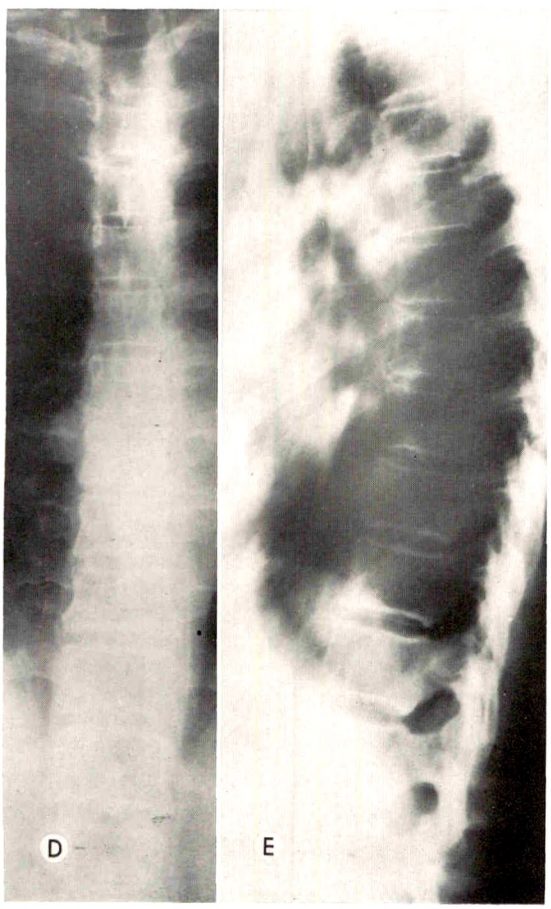


FIG. 4. (*D* and *E*) There is a normal spine.

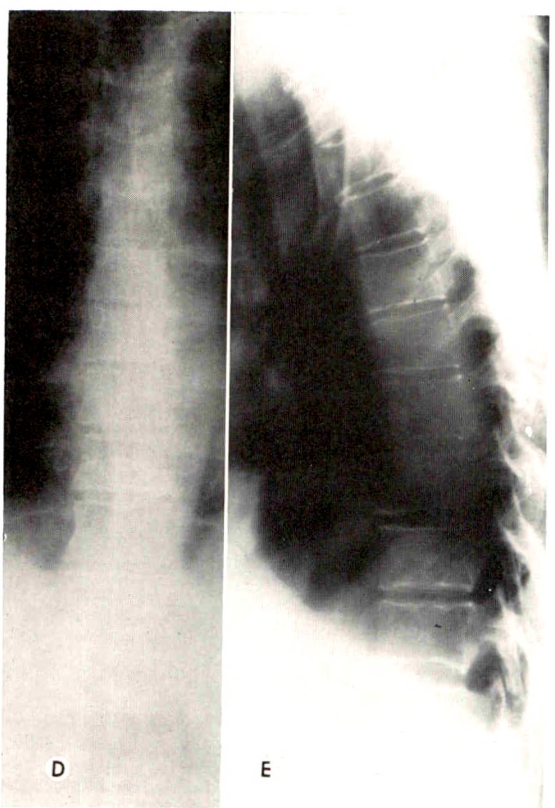


FIG. 5. (*D* and *E*) The spine shows only minimal degenerative changes.

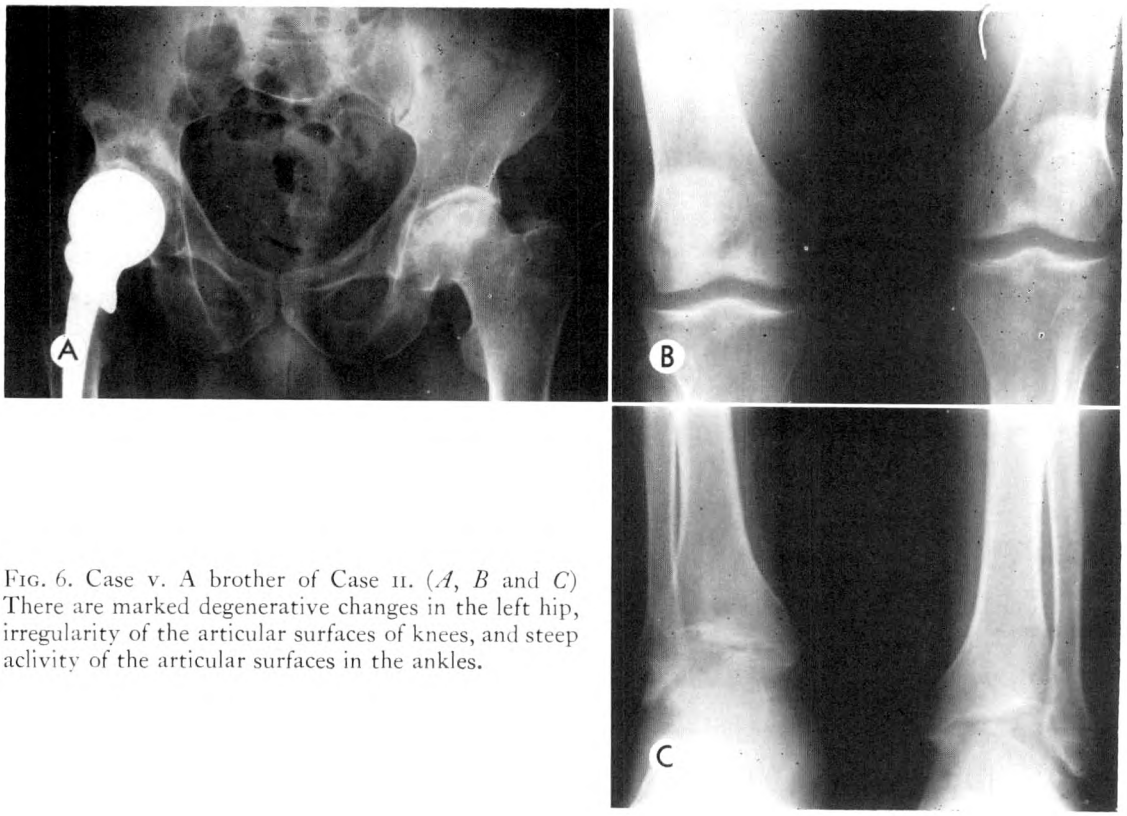


FIG. 6. Case v. A brother of Case II. (*A*, *B* and *C*) There are marked degenerative changes in the left hip, irregularity of the articular surfaces of knees, and steep aclivity of the articular surfaces in the ankles.

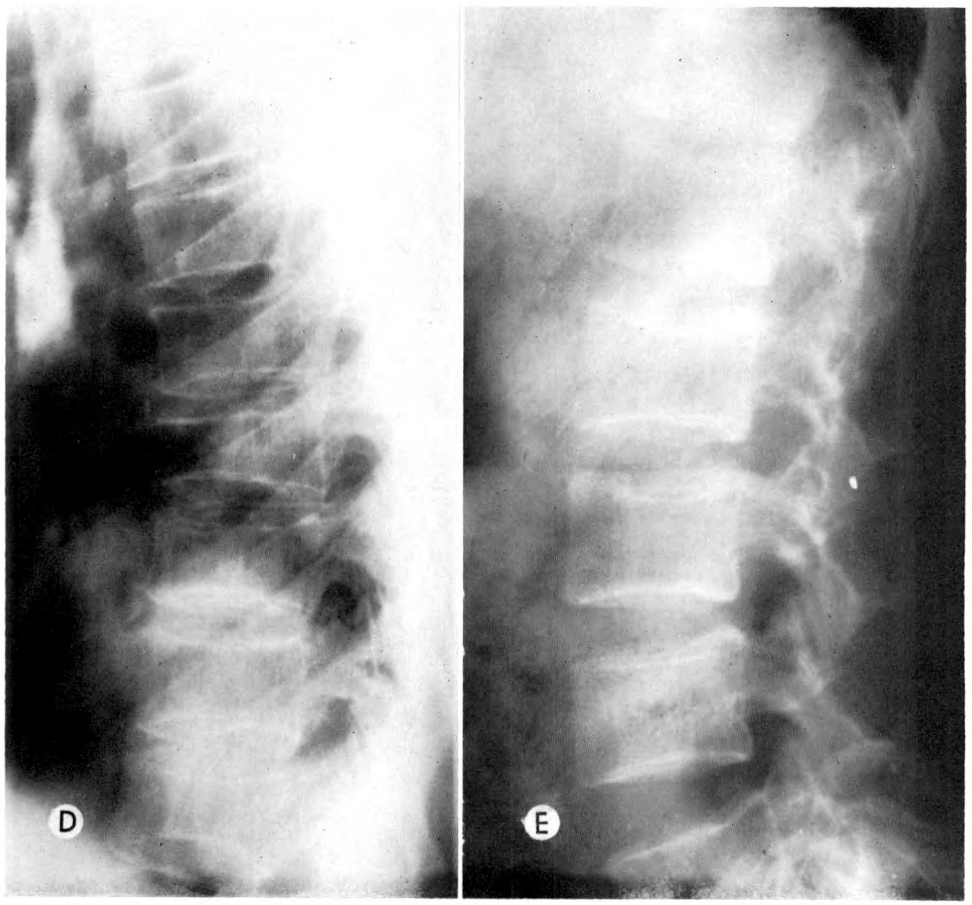


FIG. 6. (*D* and *E*) The spine only shows an old compression fracture in the dorsal region.

volvement in different individuals is also evident in this study, and is a familiar phenomenon in familial bone dysplasia.

SUMMARY

A familial study of multiple epiphyseal dysplasia is presented to indicate lack of correlation between spinal involvement and severe peripheral joint disease. Although transmitted as an autosomal dominant, there is considerable variability in the manifestations of the disease, even in a given family.

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ROENTGENOGRAPHIC MANIFESTATIONS OF HEREDITARY PERIPHERAL DYSOSTOSIS*

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SINCE Brailsford[7] first described a family with a new form of brachydactyly and coined the term "peripheral dysostosis" to separate this syndrome from others associated with short fingers, a number of authors have published similar cases.[3,4,7,15,22,27,29] From a review of this literature several salient features become apparent. First, confusion exists as to the clinical and radiologic criteria necessary to delineate the various forms of brachydactyly. Second, the genetic data supporting an autosomal dominant pattern of inheritance for peripheral dysostosis is meager. Brailsford's pedigree remains the largest familial aggregation of the disorder, even though other authors have described families with several members affected. Third, the frequent association of certain clinical features suggests that systemic disease may be present in addition to the simple brachydactyly. Furthermore, the spectrum of roentgenographic abnormalities in so-called peripheral dysostosis may indicate the need for a subclassification into several separate and distinct entities or may be a manifestation of the variation in a single entity.

The authors describe the familial occurrence of a form of brachydactyly characterized primarily by short metacarpals and metatarsals. Genetic data from two pedigrees are discussed, and the spectrum of the clinical and roentgenographic findings is presented.

REPORT OF CASES WITH ROENTGENOGRAPHIC FINDINGS

CASE I. A 14 year old white female was admitted to the University of Virginia for the evaluation of grand mal seizures. Physical examination was entirely normal with the exception of the presence of short, stubby hands and feet. A review of the family history revealed that both the mother and an older sister have short hands and feet similar to those of the patient. Routine laboratory studies were all normal including several serum calcium, phosphorus and alkaline phosphatase determinations. This patient is the propositus of Pedigree 1 (Fig. 1).

Roentgen examination of the skull, pelvis, chest and spine were normal.

The roentgenographic abnormalities in hands and feet were as follows:

Hands (Fig. 2*A*). All metacarpals are uniformly short and stout. There is deformity of the bases of the middle phalanges of the second fingers, particularly on the right suggesting old cone epiphyses. The distal phalanges of the thumbs are short.

Feet (Fig. 2*B*). The third, fourth and fifth metatarsals are short bilaterally as is the first metatarsal on the left. The phalanges are stout. The distal phalanx of the right first toe is short.

CASE II. This healthy, 16 year old sister of the propositus in Pedigree 1 was examined after obtaining the family history of short hands and feet associated with short stature. With the exception of the small hands and feet, review of her past medical history and physical findings was entirely negative. There was no history of a seizure disorder. Laboratory data including serum calcium, phosphorus and alkaline phosphatase determinations were normal. Roentgenographic examination of the skull was normal.

The roentgen examination of the hands and feet showed the following:

Hands (Fig. 3*A*). All metacarpals are markedly short with the exception of the second bi-

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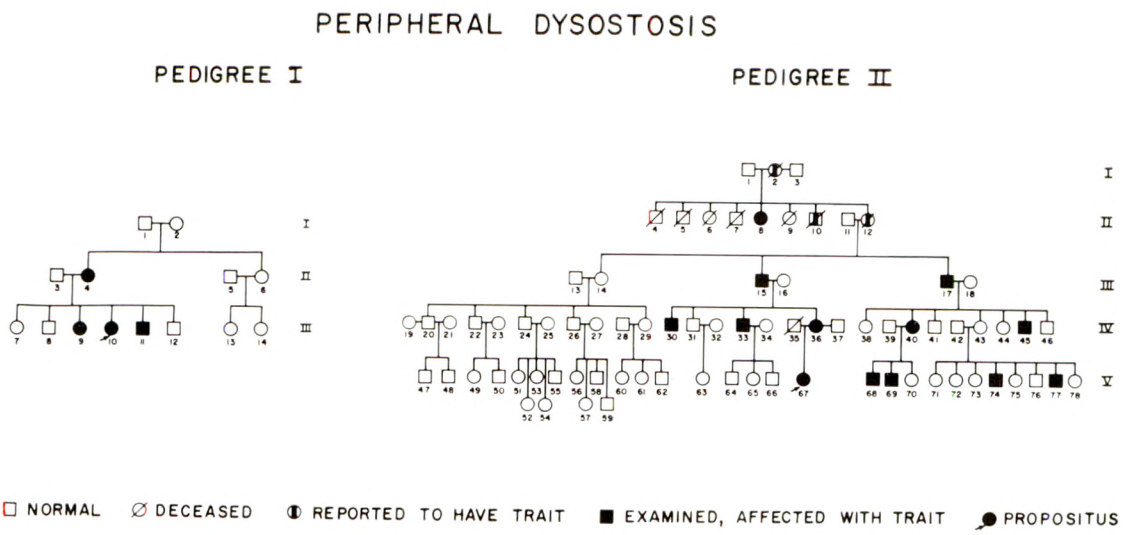


Fig. 1. The pedigrees of hereditary peripheral dysostosis. Pedigree II demonstrates an autosomal dominant pattern of inheritance for this disorder.

laterally and the third on the left which are less severely affected. The affected metacarpals are also broad. The distal phalanx of the third finger of the right hand is short and broad as are the distal phalanges of the thumbs.

Feet (Fig. 3*B*). All metatarsals are short with the first on the left and the fourth and fifth bilaterally being severely affected. The phalanges are short and stout. The bases of the proximal row of phalanges are concave, suggesting that these may have been formed from cone epiphyses.

Case III. This is the 34 year old mother of the 2 previously described cases (Case I and II). No medical abnormalities were noted either by history or physical examination. She had small hands and feet similar to her daughters'. All 3 affected members of this family were of short stature, ranging from 5 feet to 5 feet, 3 inches in height. Determinations of serum calcium, phosphorus and alkaline phosphatase were normal, as was the roentgenographic examination of her skull.

The roentgen examination of her hands and feet showed the following:

Hands (Fig. 4*A*). The first metacarpals are short and broad as are the distal phalanges of these fingers. The fifth metacarpals are short.

Feet (Fig. 4*B*). The first metatarsals are short as is the fourth metatarsal on the left foot. The phalanges are short and stout. The bases of the

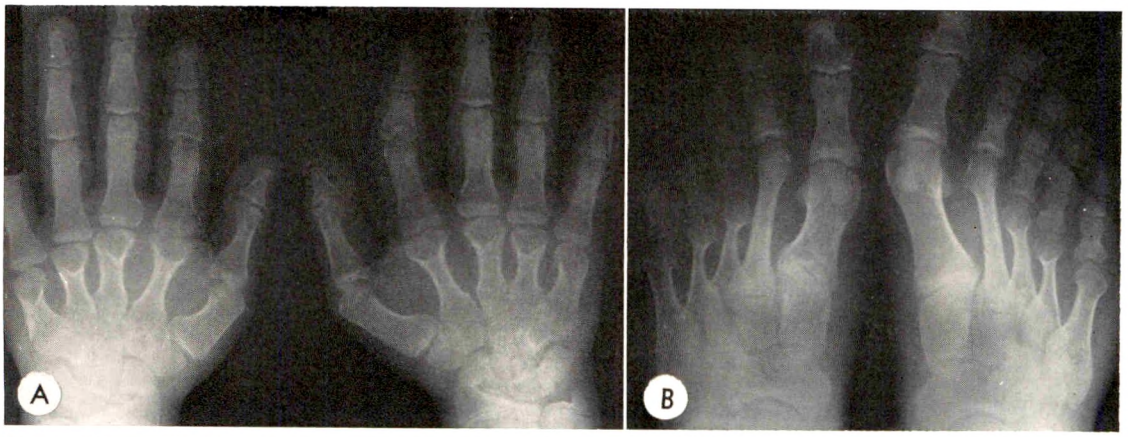


Fig. 2. Case I. (*A* and *B*) Anteroposterior views of the hands and feet of Individual III-10 in Pedigree I.

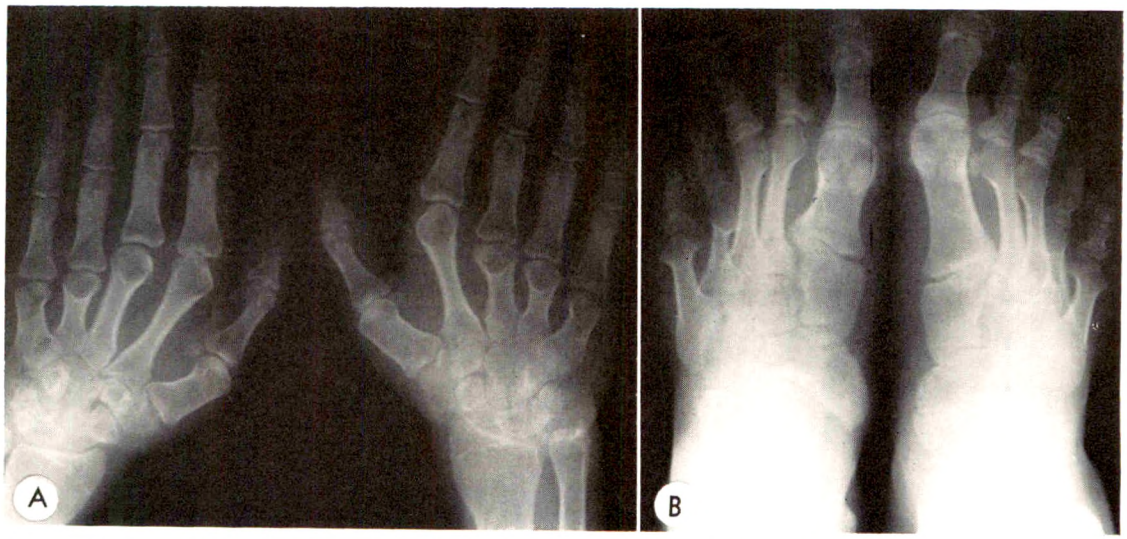


Fig. 3. Case II. (*A* and *B*) Anteroposterior views of the hands and feet of Individual III-9 in Pedigree I

first metatarsals are indented, perhaps secondary to old cone epiphysis.

Case IV. This healthy 5 year old son of Case III had a negative past medical history and demonstrated no abnormalities of his hands or feet on clinical examination. Serum calcium, phosphorus and alkaline phosphatase determinations were within the normal range.

The roentgen examination of the skull and hands (Fig. 5*A*) were normal, but roentgenograms of the feet revealed the following:

Feet (Fig. 5*B*). The metatarsals are normal in length, and no abnormalities are noted in phalangeal length. The bases of the second, third and fourth proximal phalanges bilaterally are classical examples of cone epiphyses.

Case V. A 21 year old white female (the propositus of Pedigree II) has been followed at the University of Virginia Hospital for 10 years with temporal lobe seizures. The etiology of the seizures is not clear; however, the seizures began 2 months after recovery from an episode of coma associated with measles at the age of 8 years. In addition to the neurologic disorder, the patient had a patent ductus arteriosus presently complicated by pulmonary hypertension and a reversal of the shunt. Physical examination revealed the typical findings expected as a result of her congenital heart disease, including peripheral cyanosis. She was of short stature with small hands and feet. Repeated serum calcium, phosphorus and alkaline phosphatase determinations were normal. Extensive chemical

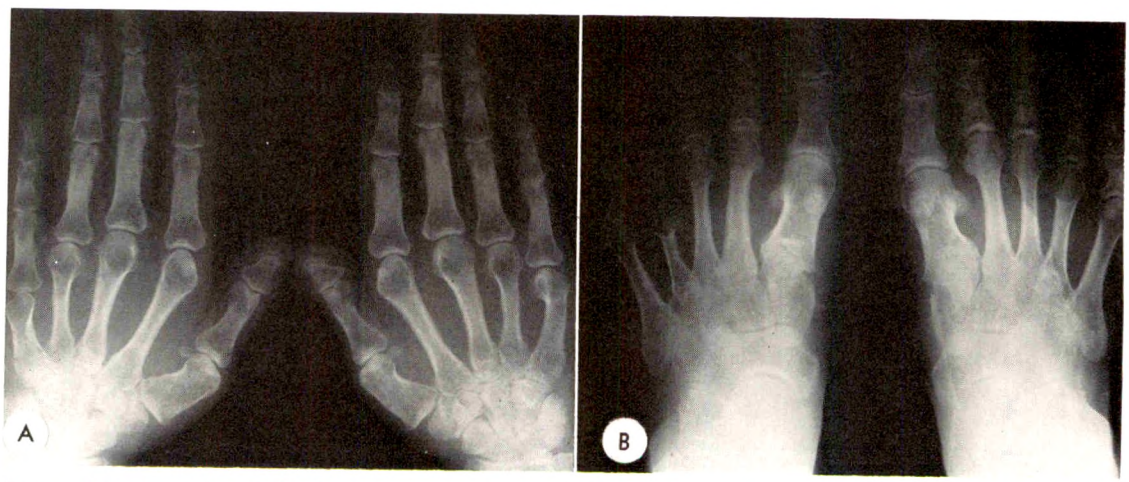


Fig. 4. Case III. (*A* and *B*) Anteroposterior views of the hands and feet of Individual II-4 in Pedigree I.

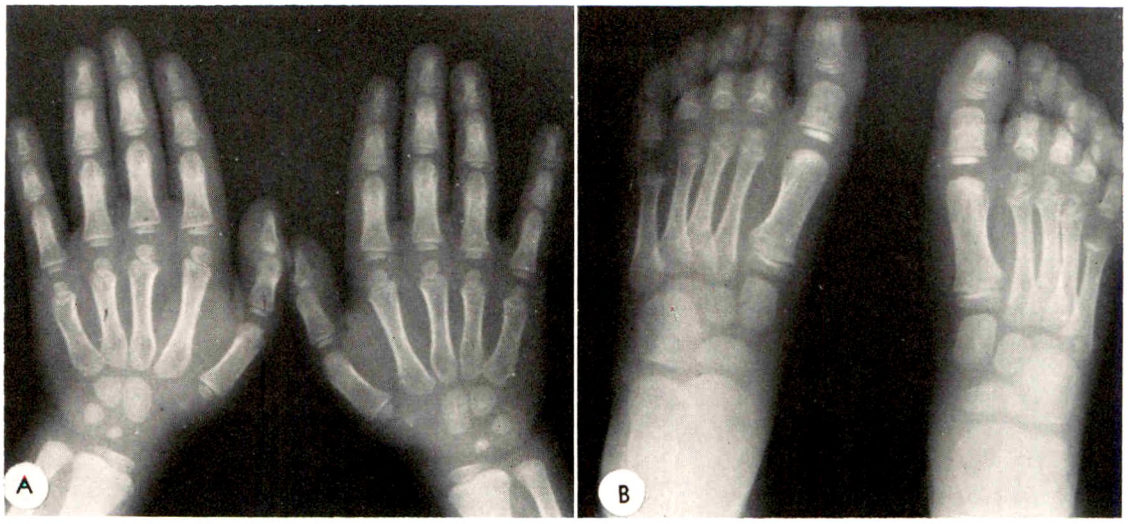


Fig. 5. Case iv. (*A* and *B*) Anteroposterior views of the hands and feet of Individual iii-11 in Pedigree i.

studies and chromosome analyses were performed in an attempt to confirm the clinical impression of a genetic or familial syndrome. No abnormalities were found except on roentgen examination. The patient refused to have her feet roentgenographed but the shortness of her feet with their grossly disproprotionate phalangeal lengths strongly implicated pathology of the feet on clinical grounds alone. Roentgen examination of the skull was normal.

The roentgenographic findings of the hands were as follows:

Hands (Fig. 6). There is marked shortening and broadening of the third, fourth and fifth metacarpals bilaterally. The middle phalanges of the second fingers and fifth fingers are short and stout. The base of the middle phalanges of the second fingers is indented suggesting old cone epiphyses.

Case vi. This healthy 36 year old mother of Cases vii and viii was detected during studies on the family members of Pedigree ii. She was of short stature and had disproportionate shortening of her fingers. She had enjoyed perfect health all her life, and no neurologic or gynecologic disease was evident by history. Her 2 sons (Cases vii and viii) were also noted to have "absent knuckles", but were otherwise in perfect health.

The results of the roentgen examination of the hands and feet of this mother and her 2 sons were as follows:

Hands (Fig. 7*A*). There is marked shortening of the fourth metacarpal and slight shortening of the fifth metacarpal of the left hand. The fifth middle phalanx on the left is short and stout. The terminal phalanges of the second, third and fourth fingers bilaterally are short and thick.

Feet (Fig. 7*B*). The feet are normal with the exception of a short first metatarsal bilaterally and concavity of the bases of the proximal phalanges.

Case vii. This is the healthy 14 year old son of Case vi.

Hands (Fig. 8*A*). The metacarpals are completely normal in both hands; however, the middle phalanges of both index fingers are short and stout with deformity of the bases suggesting old cone epiphyses. The terminal phalanges of the third fingers are short and thick. In addition, the middle phalanges of the fifth fingers are short, thick, and curved.



Fig. 6. Case v. Anteroposterior views of the hands of Individual V-67 in Pedigree ii.

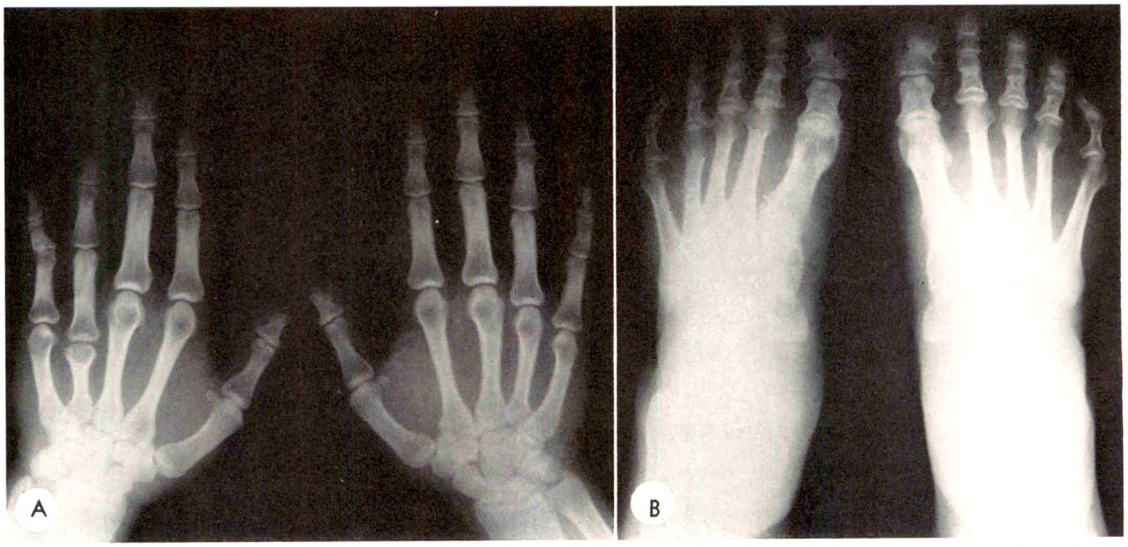


FIG. 7. Case VI. (*A* and *B*) Anteroposterior views of the hands and feet of Individual IV-40 in Pedigree II.

Feet (Fig. 8*B*). The roentgenographic appearance of the feet is normal with the exception of slight cupping of the bases of the proximal phalanges bilaterally suggesting old cone epiphyses. The fifth toes are curved.

CASE VIII. This is the healthy 12 year old son of Case VI.

Hands (Fig. 9*A*). The first, fourth and fifth metacarpals bilaterally are short and thick. The hands are otherwise normal with the exception of the terminal phalanges of the first fingers bilaterally which appear short and thick in comparison to the other terminal phalanges.

Feet (Fig. 9*B*). The feet demonstrate cone epiphyses at the bases of the proximal phalanges bilaterally. The phalanges all appear short and thick, but the most marked change is evident in the proximal phalanx bilaterally.

DISCUSSION

To segregate peripheral dysostosis from other disorders associated with metacarpal

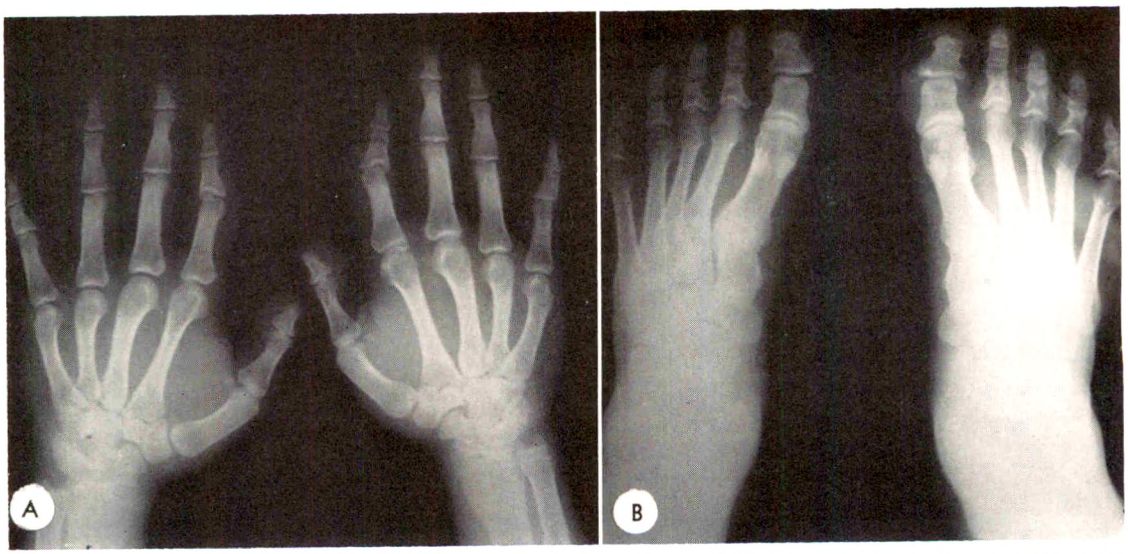


FIG. 8. Case VII. (*A* and *B*) Anteroposterior views of the hands and feet of Individual V-69 in Pedigree II.

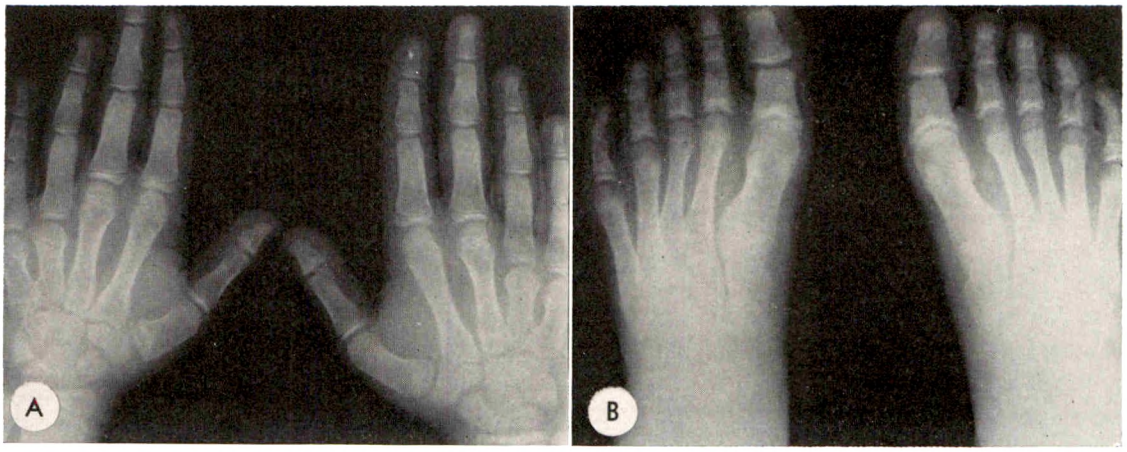


Fig. 9. Case VIII. (*A* and *B*) Anteroposterior views of the hands and feet of Individual V-68 in Pedigree II.

(MCP) or metatarsal (MT) anomalies, the following simple set of criteria is utilized by the present authors: (1) Short but not deformed metacarpal and/or metatarsal bones are present; (2) the affected individuals are short-statured, the adults are usually less than 5 feet, 5 inches tall; (3) the skeleton is otherwise normal by physical and roentgen examination (especially the skull); and (4) the serum calcium, phosphorus and alkaline phosphatase are always within the normal range.

The first criterion must be further qualified as a result of experiences gained through the roentgenographic study of the familial forms of this syndrome. In general, there is wide variation in the roentgenologic manifestations as illustrated by Figures 2*A* through 9*B*. The metacarpals and metatarsals are not deformed but are shorter and often broader than normal. Measurements must be made to define the shortness of metacarpals as compared to the proximal phalanges. At times the metacarpal shortening may be proportionate, deceiving the film reader who has not made specific measurements. In other cases, the shortening is obviously disproportionate and makes recognition of the anomaly easy.

The metacarpal sign and "phalangeal preponderance" over metacarpals should also be discussed in relation to this syndrome. When a line drawn tangential to the distal end of the heads of the fourth and fifth metacarpals extends through the head of the third metacarpal, a positive metacarpal sign is said to be present. A positive sign is classically present in Turner's syndrome, and may be found in other disorders associated with shortened fourth and fifth metacarpals such as Kleinfelter's syndrome and Steinert's disease.[16] In view of the variability of metacarpal shortening, a positive metacarpal sign may be found in peripheral dysostosis if the fourth and fifth metacarpals are shortened and the third metacarpal happens to be unaffected. Thus, a positive metacarpal sign is present bilaterally in Case VIII and only on the left in Case II, but none of the other cases demonstrate this roentgenographic sign. This serves to emphasize the rarity of solitary fourth and fifth metacarpal shortening in peripheral dysostosis in contrast to other disorders where it is somewhat more common.

"Phalangeal preponderance" over metacarpals occurs in some cases of gonadal aplasia, and we now report its presence in peripheral dysostosis. Since Kosowicz compared the length of the fourth metacarpal with the total length of the distal (DP) and proximal phalanx (PP) of the fourth finger, control data are only available for measurements of the fourth finger.[17] In normal individuals, the length of the fourth MCP does not differ from the total length of the fourth DP and PP by more than 2 mm.

In this study the second, third, fourth and fifth fingers were measured in those subjects with closed epiphyses. Utilizing these data with reference to the fourth finger only, certain facets of peripheral dysostosis are evident. First, in an individual the phalangeal preponderance may be asymmetric. As can be seen in Case VI, phalangeal preponderance is present in the left fourth digit, whereas the right fourth finger is normal. Second, these measurements clearly confirm the clinical impression that variation can occur not only within the same pedigree, but also in such genetically similar individuals as a mother and her daughters. For example, Cases I, II and III represent respectively 2 daughters and their mother affected with peripheral dysostosis. Both daughters demonstrate phalangeal preponderance in the fourth digits, but their mother does not. Third, even though control measurements of the difference between the sum of the length of the distal and proximal phalanges as compared to their corresponding metacarpals are not available for fingers other than the fourth, the data for the second, third and fifth digits indicate that phalangeal preponderance has no finger preference. Apparent from this study is the need to establish control measurements in reference to phalangeal preponderance for digits other than the fourth finger. It appears reasonable to conclude that shortened metacarpals in peripheral dysostosis unassociated with distal and/or proximal phalangeal anomalies will result in a gross disproportion between MCP length and the sum of DP and PP length.

Phalangeal involvement in peripheral dysostosis is variable. From the cases reported herein, proximal, middle and distal phalanges may be involved with no uniform pattern. The most common anomaly of the phalanges is shortening and/or a stout appearance. Case VII emphasizes the importance of the phalangeal anomalies in peripheral dysostosis. This subject has no metacarpal abnormalities, but the middle and distal phalanges of the hand are short and stout. Thus, although this case might represent the appearance of another separate and rare hand anomaly in a pedigree of peripheral dysostosis, the more likely explanation is the occurrence of peripheral dysostosis confined to the phalanges.

Other phalangeal abnormalities visualized frequently are deformed phalangeal bases and cone epiphyses. In the present series, one characteristic lesion is the marked shortening and notching of the middle phalanx of the index finger resulting in an ulnar curvature of the finger. The latter sign may be a simple and important clinical determinant for peripheral dysostosis when it is present.

The typical cone epiphyses in the feet of Case IV, without any other stigmata of peripheral dysostosis, is perhaps comparable to the situation noted previously where no metacarpal involvement occurs, but phalangeal anomalies exist. Thus, cone epiphyses, although frequently seen in other disorders (Table I) and in "normal" subjects, are a definite component of peripheral dysostosis.[4,11,12,28]

From an analysis of Pedigree II (Fig. 1), one can conclude that peripheral dysostosis is inherited as an autosomal dominant. Although primarily affected females are described in this paper, the authors examined all members of Pedigree II and found clinical brachydactyly typical of peripheral dysostosis to be present in those subjects noted to be affected in the pedigree. The preponderance of female cases referred for study perhaps represents the importance of hand appearance to the female in contrast to the male. Although permission to roentgenograph the hands was granted by only a few subjects in this pedigree, family members are able to identify those affected with the disorder, and, in fact, their name for the anomaly is "absent knuckle disease." In the large pedigree, clinical examination of the members confirms the ease with which one can identify affected individuals by the lack of a knuckle prominence. Some affected individuals demonstrate uniform metacarpal shortening in all fingers which

Table I

DISEASES MANIFESTING PHALANGEAL CONE-EPIPHYSES*

1. No recognizable cause
2. Cleidocranial dysostosis
3. Chondroectodermal dysplasia
4. Tricho-rhino-phalangeal syndrome
5. Peripheral dysostosis
6. Osteopetrosis
7. Dysplasia epiphysialis hemimelica
8. Freiberg's affliction
9. Apert's acrocephalosyndactyly
10. Phalangeal gigantism
11. Marchesani's syndrome
12. Pseudohypoparathyroidism
13. Achondroplasia
14. Multiple exostosis
15. Sickle cell dactylitis
16. Kaschim-Beck's disease
17. Thiemann's disease

* As evidenced by the number of diseases associated with cone-shaped epiphyses, the entity occurring by itself is non-diagnostic. The present authors provide evidence that complete clinical and roentgen studies of families are necessary to exclude peripheral dysostosis as a diagnosis when cone epiphyses are present.

is equally easy to ascertain because of the small, spade-shaped hand. However, Pedigree II is constructed in part on clinical evidence alone, and complete ascertainment would necessitate a roentgenographic examination of all the members of the pedigree. In Pedigree I the members are more cooperative, and clinical plus roentgen examinations of all pedigree members are available. No definitive pattern of inheritance is determined by the pedigree; however, unless skipped generations are involved, individual II-4 probably represents a new mutation and future generations will resolve the genetics.

Since the only clinical features clearly identified with peripheral dysostosis are hand anomalies and short stature, differential diagnosis includes primarily the hereditary types of brachydactyly where hand anomalies are the predominant clinical and roentgenographic feature. Of this group Bell's Type E brachydactyly is most similar to peripheral dysostosis in its roentgenographic appearance, and both disorders demonstrate autosomal dominant patterns of inheritance.[5] The obvious and frequent involvement of phalanges, the phalangeal appearance suggestive of old cone epiphyses and the peculiar notching of the bases of the middle phalanx of the index finger serve to differentiate peripheral dysostosis from Type E brachydactyly. Furthermore, neither joint hyperextensibility nor hypoplastic metacarpal epiphyses are demonstrable in the subjects with peripheral dysostosis. In the future, emphasis should be placed on a careful delineation of the roentgenographic features in the genetic types of peripheral dysostosis and Type E brachydactyly as a prelude to a more specific differentiation between these disorders.

DISORDERS CONSIDERED IN THE DIFFERENTIAL DIAGNOSIS

A somewhat arbitrary group of disorders the present authors consider in the differential diagnosis of peripheral dysostosis is presented in Table II, and a discussion of the clinical and roentgenographic features of the hereditary brachydactylies and their variants follows.

BELL'S TYPE A-1 BRACHYDACTYLY

Type A-1 brachydactyly is an autosomal dominant trait, and its primary characteristics are shortening of the middle phalanges of the hand and the proximal phalanges of the thumb and toes.[5,26] Frequently the middle phalanges are rudimentary and sometimes fusion with the distal phalanges occurs, giving the illusion of an absent middle phalanx. A predilection for severe involvement of the first and fifth finger exists. Short metatarsals and metacarpals occur in this syndrome and affect primarily the fourth and fifth finger or toe. Isolated case reports have described selective carpal bone hypoplasia, widening of the distal articular surface of the ulna and radius, and the absence of the ulnar styloid process.

TABLE II

DISORDERS CONSIDERED IN THE DIFFERENTIAL DIAGNOSIS OF PERIPHERAL DYSOSTOSIS*

Brachydactyly Type A-I	Silver's dwarfism
Brachydactyly Type B	Biemond's syndrome I
Brachydactyly Type C	Pseudohypoparathyroidism
Brachydactyly Type D	Pseudopseudohypoparathyroidism
Brachydactyly Type E	Gonadal dysgenesis
Brachydactyly Type E with renal anomalies	Kleinfelter's syndrome
Tricho-rhino-phalangeal syndrome	Marchesani's syndrome
Tabatznick's syndrome	Orodigitofacial syndrome
Myotonia dystrophica	Multiple basal cell nevi syndrome

* This is a selected group of disorders that have roentgenographic findings primarily confined to the hand. The list is not meant to be all-inclusive or to exclude disorders with roentgenographic findings in addition to those of the hand. References to the entities not described in the text are included in the bibliography.[1,2,6,9,10,12–14,18,21,23–25,30]

Congenital sixth nerve palsy associated with horizontal nystagmus is reported in a single pedigree member and Tentamy[26] raises the question of associated ocular anomalies in this disorder.

BELL'S TYPE B BRACHYDACTYLY

Another form of brachydactyly with wide variance in its expression and an autosomal dominant pattern of inheritance is Bell's Type B.[5,26] The primary features of this disorder are the complete loss or hypoplasia of the distal or middle phalanges of the hand, absent or deformed finger nails, and a flattened, split or duplicated distal phalanx of the thumb. The lesion is usually symmetric and the radial digits appear to be more severely affected than the ulnar digits. The feet demonstrate anomalies comparable to the hands, but are less severely affected. Additional components of this disorder include soft tissue syndactyly (most frequently between the second and third toes), proximal or distal symphalangism, carpal and/or tarsal fusion, short metacarpals and/or metatarsals, and thin, parchment-like skin reminiscent of the skin in the Ehlers-Danlos syndrome. Isolated case reports have also described such associated anomalies as micrognathia, renal aplasia, congenital macular coloboma, and multiple colonic polyps.

BELL'S TYPE C BRACHYDACTYLY

An autosomal dominant pattern of inheritance with a wide variability of expression characterizes this disorder.[5,26] The full expression of the malformation includes the clinical appearance of the hand with the ring finger predominating in length, brachymesophalangy of the index, middle and little finger, hyperphalangy of the index and middle finger, a short first metacarpal and deformity of the proximal phalanx of the index finger, causing ulnar deflection of the finger. These deformities may be symmetrical and bilateral or can be non-symmetric and unilateral. In addition, other anomalies may be associated with the disorder including the following: short metacarpals other than the first, odd-shaped metacarpals (circular or triangular), tibia vara, a widened and/or irregular distal end of the radius, partial or complete fusion of the trapezium and trapezoid, clinodactyly of the fifth fingers, malformed phalangeal epiphyses, and simean creases. The feet may or may not be affected, and shortened metatarsals, brachymesophalangy, and shortened proximal phalanges have been described. Other anomalies such as symphalangism, pedunculated post-minimi, arachnodactyly, macrophalangy, talipes valgus and short stature may be present.

A variant of this type of brachydactyly is reported to be associated with abnormalities of the capital femoral epiphyses and unusual dermatoglyphic patterns.[19] The number of abnormalities associated with this form of brachydactyly emphasizes the need for study of pedigrees with this and similar disorders and the inclusion of dermatoglyphic analyses.

BELL'S TYPE D BRACHYDACTYLY

This form of heritable brachydactyly has an autosomal dominant pattern of inheritance and is characterized by a short, broad thumb.[5,26] The malformed thumb may be either unilateral or bilateral, and frequently the base of the terminal phalanx is broader than the surface of the proximal phalanx with which it articulates. Other anomalies associated with this disorder are short, stubby first toes, shortened and broad terminal phalanx of the middle finger and toe, shortened fourth and fifth metacarpals and shortened fourth metatarsal. This anomaly must be carefully differentiated from Rubinstein's syndrome, Tabatznick's syndrome, and Type B brachydactyly. Females seem to be affected in a greater proportion than males.

BELL'S TYPE E BRACHYDACTYLY

This is an autosomal dominant form of brachydactyly consisting of shortened metacarpals associated with occasional metatarsal shortening.[5,26] With few exceptions, the phalanges are normal in length and size. Other abnormalities include hypoplastic metacarpal epiphyses, short nails (especially of the thumb), joint hyperextensibility and short stature. The shortened metacarpals and metatarsals are usually asymmetric in occurrence and variable as to their finger preference. In syndromes such as Turner's, Albright's hereditary osteodystrophy, Silver's dwarfism, and Biemond's syndrome I,[1,2,6,16,18,21] the brachydactyly is classified frequently as a variant of Type E.

TYPE E BRACHYDACTYLY WITH RENAL ANOMALIES

Tentamy described 2 patients with asymmetric metacarpal shortening.[26] One of these subjects had renal aplasia associated with Klippel-Feil deformity, and the other had renal hypoplasia with shortened metatarsals as well. A number of additional malfunctions were noted in the latter case. These include incomplete atresia of the auditory canals, embryonic mesenchyme in the cavum tympani and the epitympanic recess, protruding mandible, small yellow teeth, and a high-arched palate. This association of relatively minor types of brachydactyly with renal anomalies deserves special attention since insignificant and easily missed skeletal deformities may be clues to underlying asymptomatic renal disease.

BIEMOND'S SYNDROME I

In 1934, Biemond noted the association of cerebellar ataxia, nystagmus, mental retardation, strabismus and shortened metacarpals and/or metatarsals.[6,26] No other subjects have been reported with this disorder, and further cases of this entity must be described before the full syndrome and mode of inheritance can be determined. This may be another variant of Type E brachydactyly.

SILVER'S DWARFISM

This syndrome is not yet fully defined.[21] Thus far no clear-cut pattern of inheritance has been delineated, and most cases are sporadic in occurrence. The general features of this group of patients are short stature, low birth weight, skeletal asymmetry, short fifth fingers and clinodactyly, syndactylism, and a variation in sexual development. Café au lait spots are seen in about one-half of the reported cases. The metacarpals are shortened and hypoplastic. Some of these patients have elevated gonadotrophins. This is classified by some as a variant of Type E brachydactyly.

TABATZNICK'S SYNDROME

This is a recently described heart-hand syndrome with shortening and hypoplasia of the fourth and fifth metacarpals and various cardiac abnormalities.[26] The latter are usually confined to tachycardias or conduction defects; however, one patient is known to have had a small patent foramen ovale. The upper limbs of these patients are short with a decrement in the deltoid muscle mass, and in addition, the distal end of the humerus and radius are bowed and flared. The ulnar styloid process is absent and the terminal phalanges of the thumb are short

and flat. Present evidence supports an autosomal dominant pattern of inheritance for this disorder. Recently another report of brachydactyly and heart valve disease has appeared.[8] In one reported patient, the phalanges and metacarpals are short, and the author considers the hand anomaly a variant of Bell's Type E brachydactyly. In the other patient there is hypoplasia of the hand, syndactyly, and particularly evident hypoplasia of the distal and middle phalanges. The author classifies the latter hand anomaly as Bell's Type A-I brachydactyly. Both patients are normal in height with no other known associated abnormalities except for cardiac disease. Pulmonary and aortic stenosis exist in the first patient, whereas aortic stenosis alone is present in the second case. These hand anomalies associated with cardiac abnormalities are included in this paper under the heading of Tabatznick's syndrome, since it is increasingly evident that the Bell classification needs revision.

SUMMARY

The occurrence of a genetic type of peripheral dysostosis is described. Both the extreme variation in the roentgenographic manifestations and the pedigree analyses suggest an autosomal dominant pattern of inheritance.

The roentgenographic examination demonstrates all the features discussed in previous publications, and the genetic studies emphasize the heterogeneity of the roentgenologic findings.

For the present, the variability with the clearly genetic types strongly implicates a single entity, peripheral dysostosis, as responsible for the diversity. Cone-shaped epiphyses, short phalanges, short metacarpals, short metatarsals can occur as isolated phenomena, but further family studies may bring the spectrum of peripheral dysostosis into perspective. One other component of this disorder, the short stature, is a constant feature in affected individuals.

The genetic diversity of peripheral dysostosis may obviate the necessity of subclassification; however, the presence of clinical symptoms and signs in affected individuals as yet poorly classified in relation to the brachydactyly itself may provide a need for further separation of this seemingly single disease.

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THE ACETABULAR ANGLE IN HUMAN FETUSES*

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CAFFEY *et al.*[1] have demonstrated the wide variation of the acetabular angle in newborn infants, as measured by the Hilgenreiner[2] method. They found the range to be from 10° to 44°. The mean values for acetabular angles of all categories of newborns whom they examined varied between 29° and 25° and the 2 Standard Deviation ranges were 39° to 20° and 34° to 16°, respectively. The acetabular angle decreases with age. According to Wilkinson and Carter,[3] the mean acetabular angle decreases from a mean value of 24.5° for boys and 24.7° for girls at the age of 6 months to 14.7° and 15.9° respectively at the age of 36 months. The approximate 2 Standard Deviation range was ±9.1 at 6 months, and ±7.2 at 36 months.

But is the acetabular angle measurable before term? In roentgenograms taken during the latter stages of pregnancy (for reasons unconnected with the present study) we were unable to delineate the angle. We, therefore, made roentgenograms of 7 preserved fetuses, whose estimated ages ranged from 21 to 27 weeks; the crown-heel length (standing height) ranged from 25 cm. to 35 cm. (Table 1). They had been fixed in formalin and thereafter kept in a 3 per cent phenol solution and had a hard rubber consistency. The roentgenograms (Fig. 1) were taken with an exposure of 40 kv. and 6 mas. at a focus film distance of 90 cm., without a grid. The back of the fetus was laid straight on the table and the hips were forcibly extended. No attempt was made to correct the prevalent hip abduction.

Each acetabular angle was measured 3 times, at intervals, on the same roentgenogram and by the same investigator. This was done by delineating the angle on transparent paper placed over the roentgenogram; a fresh drawing was made for each measurement. The findings are shown in Table 1. The differences between the successive measurements (*i.e.*, the personal error) ranged from 0° to 9°. In 4 of the specimens, the acetabular angles (both right and left) were measured also in enlarged photographs of the roentgenograms (Fig. 2), in order to see whether the measurements differed materially from those made on the original roentgenograms. The personal error was found to range from 0° to 7°. The difference between the means of the 3 successive measurements, as made on the original roentgenograms, and those made on the enlarged photographs ranged from 0° to 5°. Thus, the use of enlarged photographs, although it facilitated measurements, did not significantly improve the accuracy and the final results were also not markedly different.

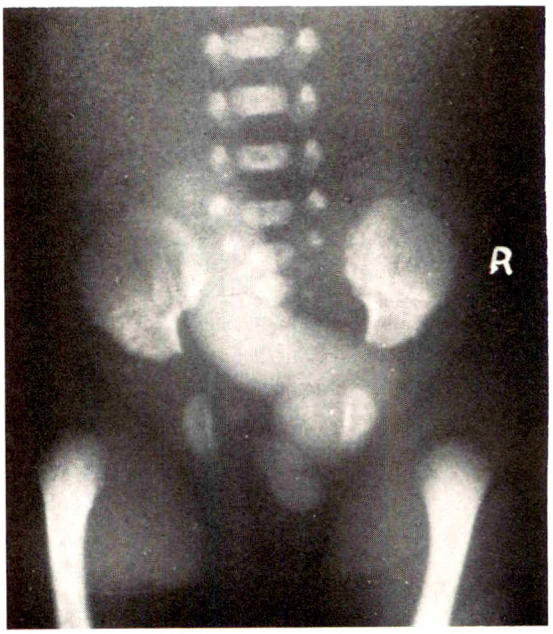


FIG. 1. Roentgenogram of Fetus A (see Table 1). Mean acetabular angle 30° (right), 25° (left).

It will be seen from Table 1 that the

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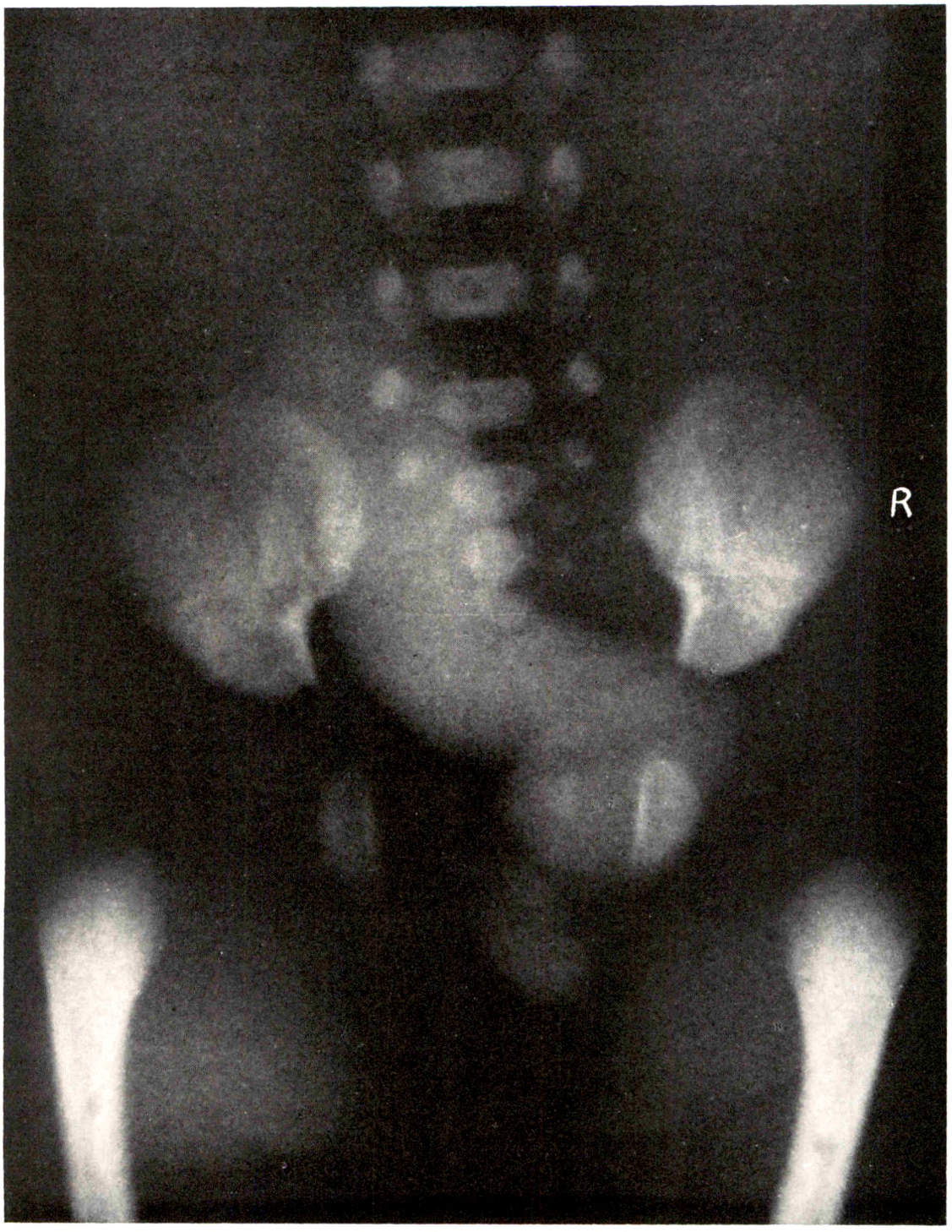


Fig. 2. Enlarged photograph of roentgenogram of Fetus A (Fig. 1).

TABLE I

THE ACETABULAR ANGLE IN FETUSES, AS MEASURED ON THE ORIGINAL ROENTGENOGRAMS

No. of fetus	Crown-heel length; "standing height" (cm.)	Estimated age (weeks)	Sex	Right acetabular angle (degrees)		Left acetabular angle (degrees)	
				Successive measurements	Mean	Successive measurements	Mean
A	25	21	M	33, 31, 25	30	28, 26, 21	25
B	26	21	F	21, 23, 25	23	23, 26, 24	24
C	28	22	M	22, 27, 20	23	20, 20, 27	22
D	28	22	F	24, 27, 30	27	24, 27, 31	27
E	31	24	M	22, 19, 28	23	25, 30, 24	26
F	31	24	F	22, 23, 21	22	27, 27, 24	26
G	35	27	F	23, 26, 27	25	18, 24, 21	21

acetabular angle (mean of 3 measurements made on the original roentgenograms) ranged from 21° to 30°. The number of specimens was not sufficient for statistical analysis for age and sex, or for comparing the left with the right hip joint. However, all values were within the limits found by Caffey *et al.*[1] in their study of newborns.

CONCLUSIONS

It is possible to measure the acetabular angle in fetuses, at least from the age of 21 weeks.

The size of the acetabular angle, as measured in fetuses 21 to 27 weeks old, was found to be similar to that in newborn infants. This may signify that there is relatively little change in the pattern of ossification at the caudal portion of the ilium, during intrauterine life, from the end of the 5th month onwards.

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THE ROENTGENOLOGIC FEATURES OF HEMOPERITONEUM IN THE NEWBORN*

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HODGE[9] in 1870 reported the first case of fatal hemorrhage from the liver in an infant 2½ days old, but it was not until 1934 that Rogers[13] described the first case diagnosed during life. The incidence of visceral hemorrhage in the newborn, has been estimated from postmortem reviews, and bleeding from the liver accounts for 1.2 per cent[11,12] to 9.6 per cent[4] of all neonatal deaths. In our series of 809 consecutive autopsies performed on newborn babies, 20 were found to have died of bleeding from the liver (2.5 per cent) and a further 6 from other intra-abdominal viscera, giving an over-all autopsy incidence of 3 per cent. This autopsy series does not include stillbirths.

Previous reports on this subject have been either postmortem reviews or isolated cases with bleeding from specific organs. The purpose of this paper is to focus attention on this condition as a clinical entity rather than a postmortem finding and to show how roentgenologic examination confirms the clinical diagnosis and assists in localizing the site of the bleeding.

MATERIAL

Fifty-two infants with hemoperitoneum encountered at the Red Cross War Memorial Children's Hospital, Cape Town, during the 10 year period, 1957 through 1966 have been studied. This includes: (a) a retrospective study of 17 infants admitted from 1957 through 1961; and (b) a prospective study of 35 infants seen from 1962 through 1966.[6]

The various sources of intraperitoneal bleeding in this series are listed in Table I.

Table I

HEMOPERITONEUM IN THE NEWBORN—52 CASES

Sites	
Liver	32
Spleen	5
Liver and spleen	1
Suprarenal	8
Renal	4
Gastrointestinal	2

Subcapsular hematoma of the liver accounted for 66 per cent of all intra-abdominal hemorrhages.

CLINICAL FEATURES

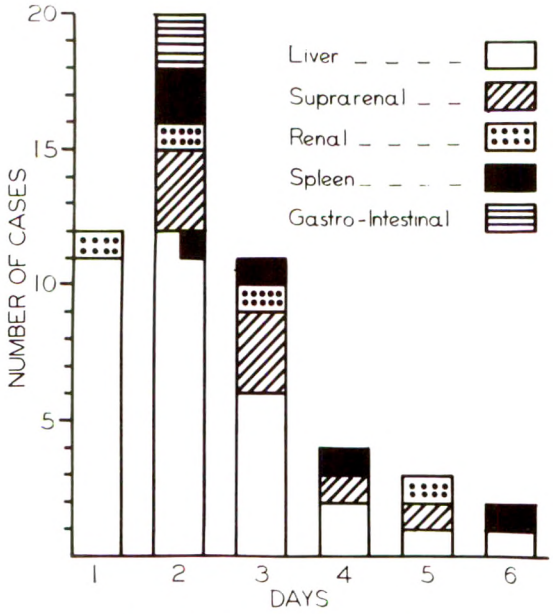
Thirty-five cases were males and 17 were females.

Hemoperitoneum rarely occurs *in utero*, not infrequently immediately after birth, but most commonly between the second and fifth days of life.[3,7] In this series 73 per cent presented between the 2nd and 5th days with the highest incidence on the 2nd day of life (Graph 1). Half the cases presented on the 1st day were premature—48.1 per cent weighed 8 lbs., 36.5 per cent between 5 and 8 lbs. and 15.4 per cent below 5 lbs. (Graph II).

A clinical diagnosis of hemoperitoneum was made in 40 of the 52 babies. In these 40 cases the first symptom noticed in every infant was a sudden onset of pallor, followed by grunting respiration and collapse in 34. An isolated vomiting occurred in 5 infants, but was not significant except in the 2 cases with subserosal hematoma of the duodenum.

The striking features on examination

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GRAPH I. Age at presentation.

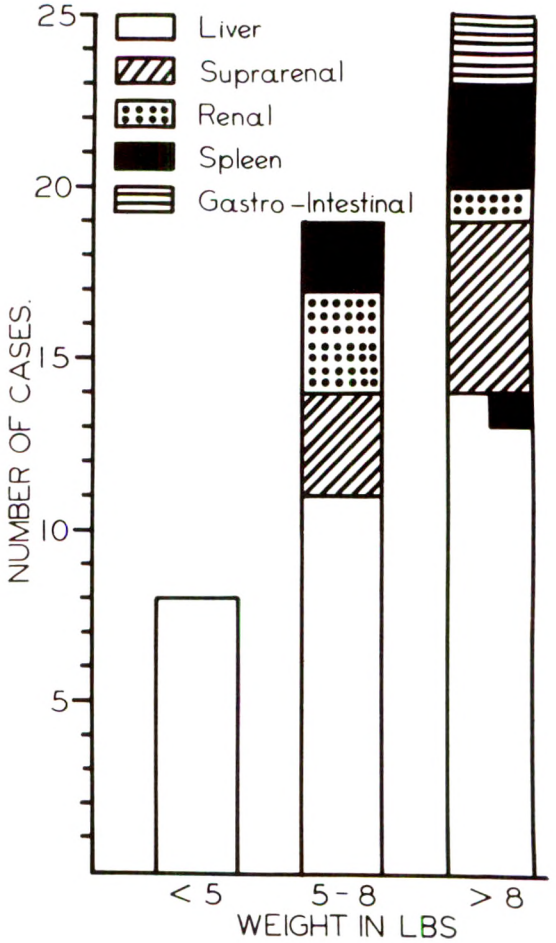
were the extreme pallor and shock, hypothermia, tachycardia and tachypnea. Significant abdominal distention was found in 95 per cent and in 80 per cent a mass was palpable. Clinical evidence of free fluid in the peritoneal cavity was detected in only 52.5 per cent. In 5, blood filled a patent inguinal sac (Fig. 1).

In this series 30 per cent had clinical evidence of bleeding elsewhere.

ROENTGENOLOGIC FEATURES

Supine and erect anteroposterior roentgenograms of the abdomen were taken routinely, and an erect lateral roentgenogram was often helpful. Medium speed screens were favored rather than high speed screens to obtain better definition. The presence of free fluid in the peritoneal cavity of all the infants was confirmed and in the majority (80 per cent) of the cases the site of the bleeding was localized.

Ninety-five per cent of the cases had abdominal distention. Other causes of distention such as cysts or ascites are not associated with shock and evidence of blood loss, and rupture of a hollow viscus would produce roentgenologic evidence of free intraperitoneal gas.



GRAPH II. Weight at presentation.

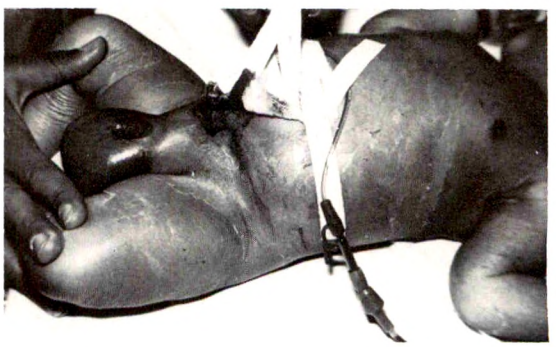


FIG. 1. Clinical picture of a 2 day old infant with hemoperitoneum being resuscitated via an umbilical vein catheter. Note the abdominal distention and the bruising of the subcutaneous tissues in the left iliac fossa. The scrotum is black from blood filling patent inguinal hernial sacs.

The roentgenologic features of free fluid (blood) in the abdomen noted in our cases were:

(1) Generalized haziness of the abdomen. This homogeneous grayness of the abdomen obscured abdominal detail and threw a veil across the gas in the bowel.

(2) The "frog belly" appearance of fullness in the flanks in the supine roentgenogram produced by the fluid accumulating there.

(3) In many of the cases there was a paucity of gas shadows in the bowel with a tendency to central localization in the supine roentgenogram, and in the erect roentgenogram a tendency for the bowel shadows to float upwards.[10]

(4) The bowel shadows showed some thickening of their walls with separation of individual loops, as would be expected with free intraperitoneal fluid.

(5) The flank sign of extraperitoneal fat, which according to Friemann-Dahl[8] may be curved and sharply defined with fluid in the flanks, was not found to be of help—probably from lack of extraperitoneal fat in these newly born infants.

ROENTGEN LOCALIZATION

Sieber and Girdany[14] in describing 3 cases of rupture of the spleen in newborn infants state that accurate identification of liver or spleen as the source of intraperitoneal hemorrhage was not possible. This was not our experience and we were able to obtain some localization in 80 per cent of our cases, although this was in retrospect in approximately 20 per cent.

Difficulty was encountered in localization when the intraperitoneal bleeding was excessive, obscuring the fixed point land marks in the abdomen. The cases where localization could be made showed an opaque mass in the bleeding area with displacement of adjacent fixed point bowel gas shadows.

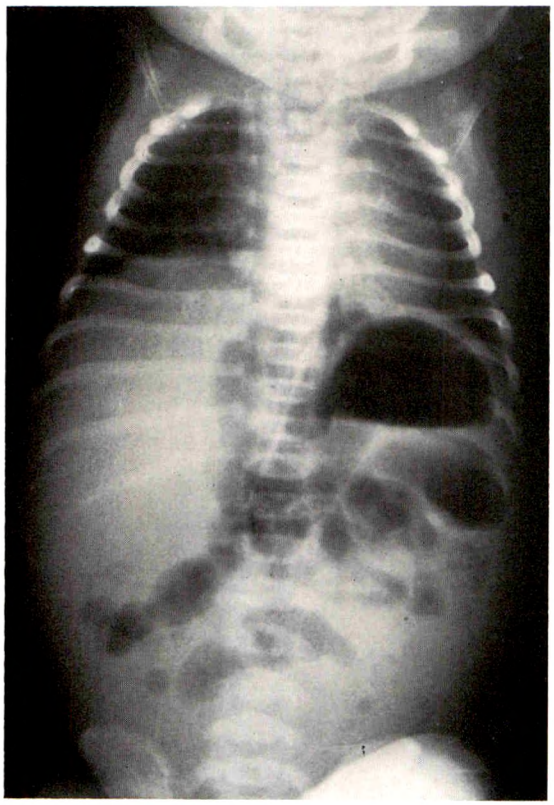


Fig. 2. Case 1. Roentgenogram of the abdomen in an infant with hemoperitoneum due to a ruptured subcapsular hematoma of the right lobe of the liver (see text).

The following cases serve to illustrate these points:



Fig. 3. Case 1. Ruptured subcapsular hematoma on the inferior surface of the right lobe of the liver at laparotomy. The free blood in the peritoneal cavity has been evacuated.

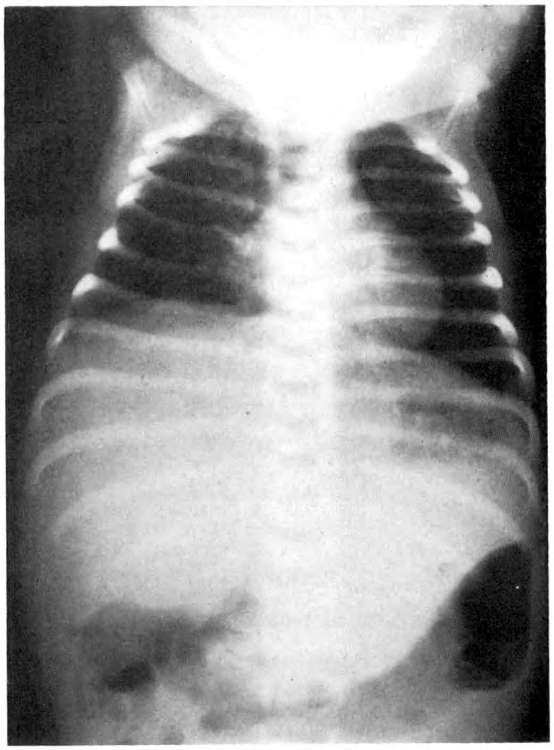


FIG. 4. Case II. Roentgenogram of the abdomen in an infant with hemoperitoneum due to a ruptured subcapsular hematoma of the left lobe of the liver (see text).

REPORT OF CASES

CASE I. (Fig. 2 and 3). A newborn infant, B.H., aged 1 day with a ruptured subcapsular hematoma of the right lobe of the liver. The erect roentgenogram of the abdomen shows bulging flanks with free fluid in the peritoneal

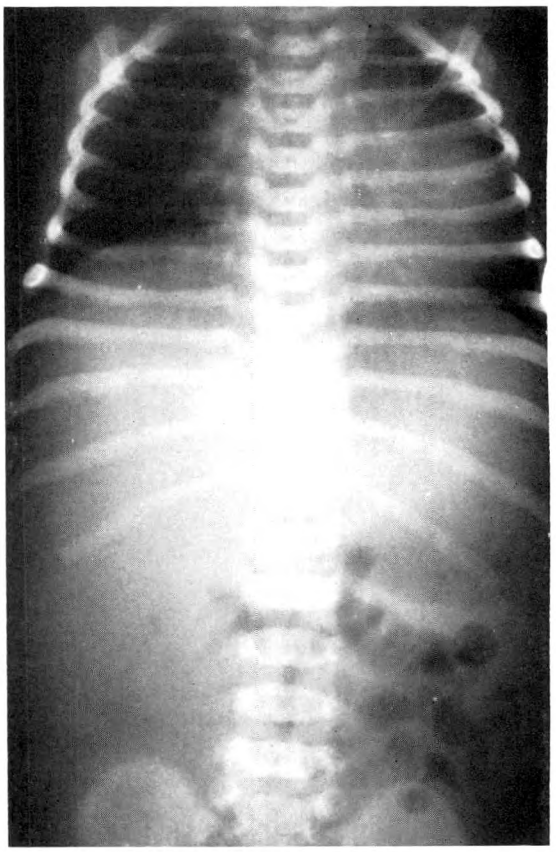


FIG. 6. Case IV. Roentgenogram of the abdomen in an infant with hemoperitoneum due to a ruptured right perisuprarenal hematoma (see text).

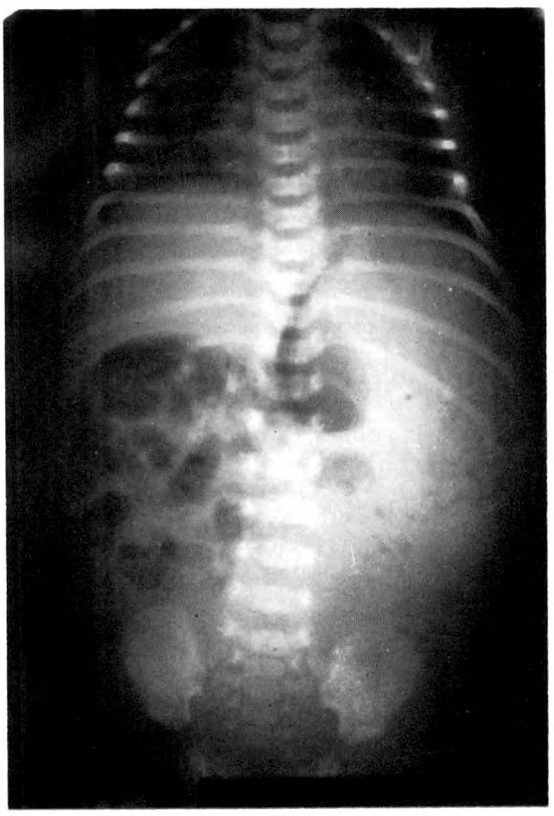


FIG. 5. Case III. Roentgenogram of the abdomen in an infant with hemoperitoneum due to a ruptured subcapsular hematoma of the spleen (see text).

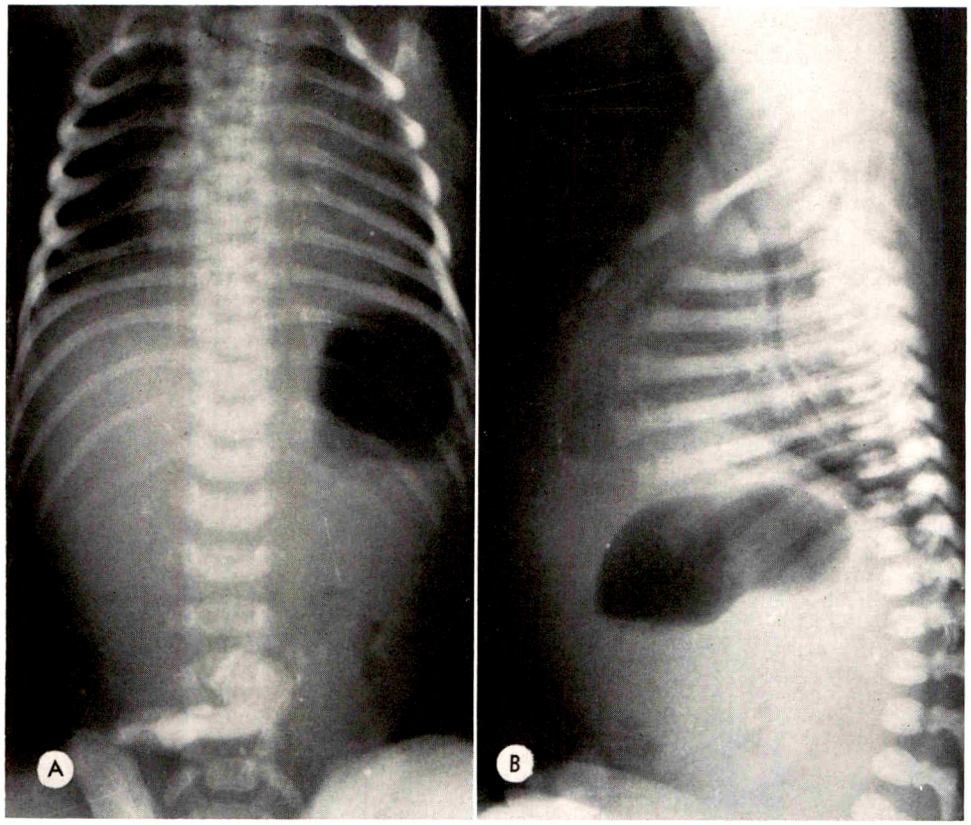


Fig. 7. Case v. (*A*) Anteroposterior roentgenogram of an infant with hemoperitoneum due to a ruptured subserosal hematoma of the duodenum. (*B*) Erect lateral roentgenogram of the same infant (see text).

cavity. There is an opaque mass in the right upper quadrant from the right lobe of the liver which is depressing the ascending colon and hepatic flexure downwards and to the left.

Case ii. (Fig. 4). An infant, F.J., aged 2 days with hemoperitoneum due to a ruptured subcapsular hematoma of the left lobe of the liver. The erect roentgenogram shows free fluid giving a generalized haze to the abdomen; there is some generalized enlargement of the liver shadow with an opaque mass in the left upper quadrant which is depressing the left transverse colon downwards.

Case iii. (Fig. 5). J.B., aged 3 days, with hemoperitoneum from a ruptured subcapsular hematoma of the spleen. The erect roentgenogram of this infant shows free fluid in the abdomen with some separation of the bowel gas shadows. There is an opaque mass in the left upper quadrant which is displacing the stomach gas shadow to the right. In addition the majority of the small bowel shadows are displaced to the right by an accumulation of blood on the left which is causing the flank to bulge on this side.

Case iv. (Fig. 6). S.P., aged 3 days, with hemoperitoneum from a ruptured right suprarenal subcapsular hematoma. The supine roentgenogram shows free fluid in the peritoneal cavity with a relative paucity of gas shadows which show separation of bowel loops. There is an opaque mass in the right loin which displaces the bowel shadows to the left. This was due to a ruptured right perisuprarenal hematoma which was filling the whole of the right loin.

Case v. (Fig. 7, *A* and *B*). B.M., aged 2 days, with a ruptured subserosal hematoma of the 4th part of the duodenum. The anteroposterior erect roentgenogram (Fig. 7*A*) shows relatively little peritoneal fluid. A fluid level is seen in the stomach area with only a few bowel gas shadows indicating obstruction. The lateral erect roentgenogram (Fig. 7*B*) shows the double fluid level indicating duodenal obstruction.

CASE VI. (Fig. 8). D.J., aged 2 days, with hemorrhage from a subcapsular hematoma of the right lobe of the liver. The supine roentgenogram shows haziness of gas shadows with some separation of the loops. There is a paucity of bowel shadows but those present are floating up centrally. The excessive amount of free fluid (blood) in the peritoneal cavity makes accurate localization of the exact site of bleeding impossible.

SPECIAL INVESTIGATIONS

The striking features in these cases were severe hypoprothrombinemia and marked acidosis.

DIAGNOSIS

With the "classical" clinical presentation, the roentgenologic signs and the blood picture, a confident diagnosis of hemoperitoneum can be made, and very often the exact site of the bleeding can be determined. Routine abdominal paracentesis has not been found necessary because the clinical presentation is so characteristic that it is hardly ever mimicked by other conditions.

DISCUSSION

An underlying hemorrhagic tendency, potential or overt, has been shown to be the basic etiologic factor with minor forms of trauma acting as the precipitating factor. The bleeding tendency has been shown to be due to a vitamin K dependent coagulation defect.[6] The detailed management of the cases in this series has been discussed in a previous publication.[6]

A clinical diagnosis of hemoperitoneum was made in 40 of the 52 infants. Thirteen were managed conservatively with only 3 survivors, whereas 23 of the 27 infants operated on survived. As a result of our experience we have found that surgical intervention is indicated, but only when the baby has been resuscitated and the underlying hemorrhagic disease has been treated. Before the coagulation defect has been corrected by the administration of vitamin K_1, *i.e.*, before the prothrombin index has risen to 60 per cent or higher, the baby must be treated like an over-ripe tomato; *viz.* no nasogastric intubation, or excessive handling should be done except for the insertion of a catheter into the umbilical vein for taking blood samples and for resuscitation. It has been shown that vitamin K_1 is safe[2,5,15] and is effective for correcting some of the abnormal coagulation defects in the newborn and its widespread prophylactic use towards the end of pregnancy should be encouraged.

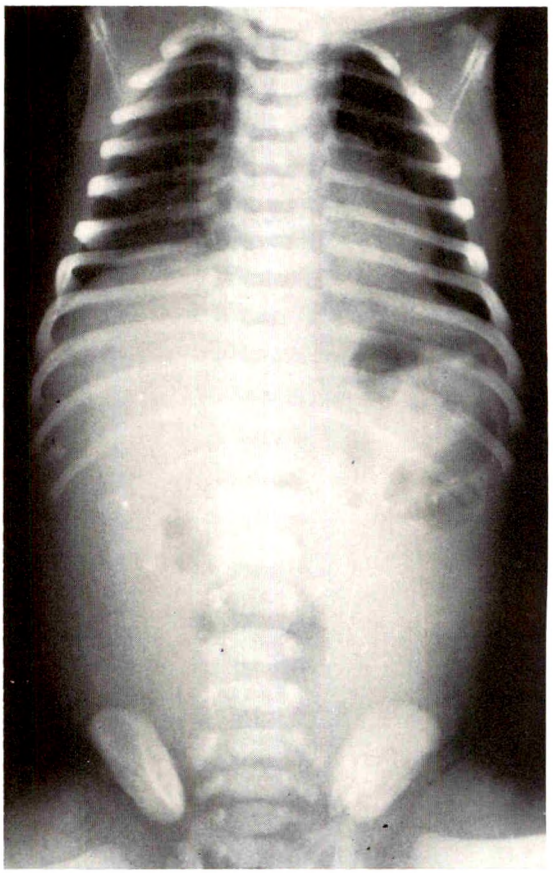


FIG. 8. Case VI. Roentgenogram of an infant with hemoperitoneum due to a ruptured subcapsular hematoma of the right lobe of the liver, but excessive blood in the peritoneal cavity obscures the exact site of bleeding.

"Those entrusted with the care of newly born infants still see many who are doomed to an early death or permanent disability, from congenital malformations or birth injuries. As years go by, the list of apparently hopeless disorders grows shorter, but it is still wise to sift it repeatedly in search of

yet others capable of responding to early diagnosis and treatment."[1]

SUMMARY

A study of 52 cases of hemoperitoneum in the newborn encountered at the Red Cross War Memorial Children's Hospital, Cape Town, during the 10 year period 1957 through 1966 is presented.

Specific roentgenologic features are described and illustrated, and their value in making a correct clinical diagnosis is stressed.

The role of a vitamin K dependent bleeding tendency and trauma as etiologic factors is mentioned in addition to the results of treatment.

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INFANTILE HEPATIC HEMANGIOENDOTHELIOMA*

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HEMANGIOENDOTHELIOMA of the liver is a rare neoplasm which may be responsible for hepatomegaly and congestive heart failure in infancy. The tumor consists of blood containing sinusoidal channels lined by proliferating endothelial cells. These cells may also form compact masses in portions of the neoplasm. We have recently seen an infant with this condition whose roentgenograms demonstrated calcifications in the right upper quadrant. This finding led us to suspect a hepatic neoplasm and angiography confirmed the diagnosis.

Our purpose in reporting this case is to call this unusual lesion to the attention of radiologists since awareness of its existence could lead to prompt diagnosis and therapy.

REPORT OF A CASE

S.M., a Caucasian female, was born on April 16, 1966, after an uncomplicated pregnancy and delivery. The birth weight was 7 pounds, 6 ounces. The infant breathed spontaneously, but soon after birth became dyspneic and cyanotic. A diagnosis of congenital heart disease was made and digoxin and oxygen were prescribed. At 4 days of age she was transferred to University of Iowa Hospitals.

On admission, the infant was noted to be dusky and to have tachycardia and tachypnea. There was a loud precordial systolic murmur and the liver was greatly enlarged. A chest roentgenogram revealed cardiac enlargement. She was treated with oxygen, diuretics and maximal dosages of digoxin and her condition remained stable. Serial roentgenograms revealed persistence of cardiomegaly and on one of these subsequent chest roentgenograms a large segment of the abdomen was included, revealing hepatomegaly with suggestion of faint right upper quadrant calcifications (Fig. 1). Abdominal roentgenograms were then obtained and confirmed the presence of hepatic calcifications (Fig. 2).

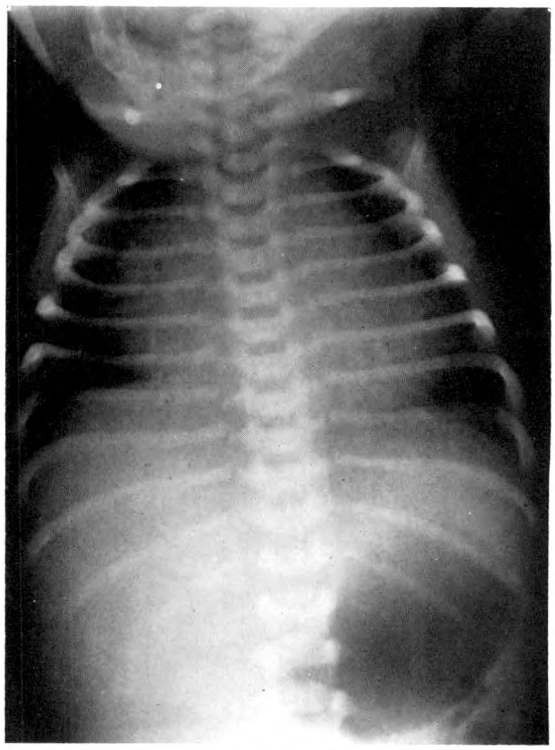


FIG. 1. Roentgenogram of the chest showing cardiomegaly and hepatomegaly. On the original roentgenogram right upper quadrant calcifications could be faintly seen.

At 16 days of age, cardiac catheterization and angiocardiography were performed. These studies revealed marked pulmonary hypertension with elevation of right and left ventricular diastolic pressures. Atrial and systemic venous pressures were also elevated. These findings were all believed to be related to cardiac failure. An atrial septal defect with bidirectional shunt was found, with the right to left component being larger than the left to right. There was also left ventricular enlargement with an intact interventricular septum and a small patent ductus arteriosus.

Abdominal aortography was performed at

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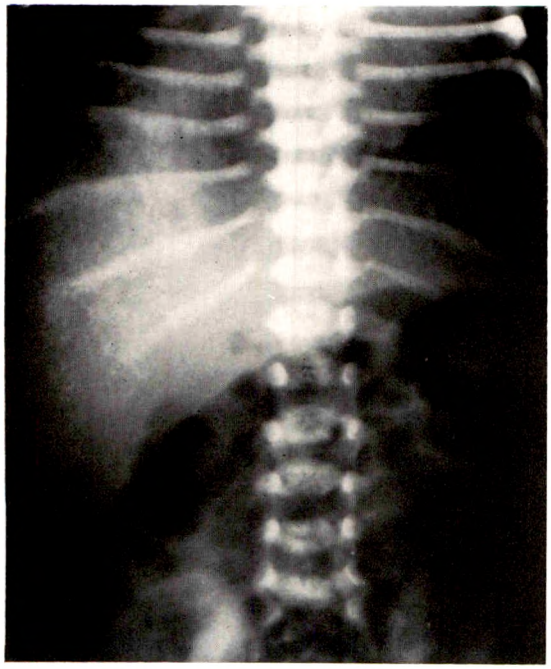


Fig. 2. Roentgenogram of the abdomen demonstrating extensive fine calcifications within the right lobe of the liver.

the same time. The early roentgenograms demonstrated enlargement of the celiac artery which gave rise to a very large hepatic artery. Other smaller arteries entered the liver from the aorta (Fig. 3*A*). Later roentgenograms revealed filling of a large angiomatous lesion of the right lobe of the liver (Fig. 3*B*). Several hours after the angiographic studies and before surgical therapy could be instituted, the patient developed deep cyanosis, bradycardia and rapidly expired.

Postmortem examination revealed a hemangioendothelioma of the right lobe of the liver (Fig. 4), cardiac enlargement, atrial septal defect and a probe patent ductus arteriosus. No visceral or cutaneous hemangiomata were found. The cause of death was cardiac failure secondary to the large volume shunt through the hepatic tumor. The atrial septal defect and small patent ductus arteriosus were not believed to be significant contributing factors.

DISCUSSION

Infantile hepatic hemangioendothelioma is almost exclusively a lesion of the first 6 months of life.[1,16] This tumor is generally considered to be a benign lesion, although malignancy may be suggested histologically.[1,2,4] In spite of the rarity of metastasis, the neoplasm has been associated with a high mortality in the infantile period. Cardiac failure secondary to large volume extracardiac shunting of blood is the most common cause of death.[3,4,8,16] Fatal hemorrhage from the tumor or from associated capillary hemangiomas of the gastrointestinal tract has also been reported.[2,6,7] Spon-

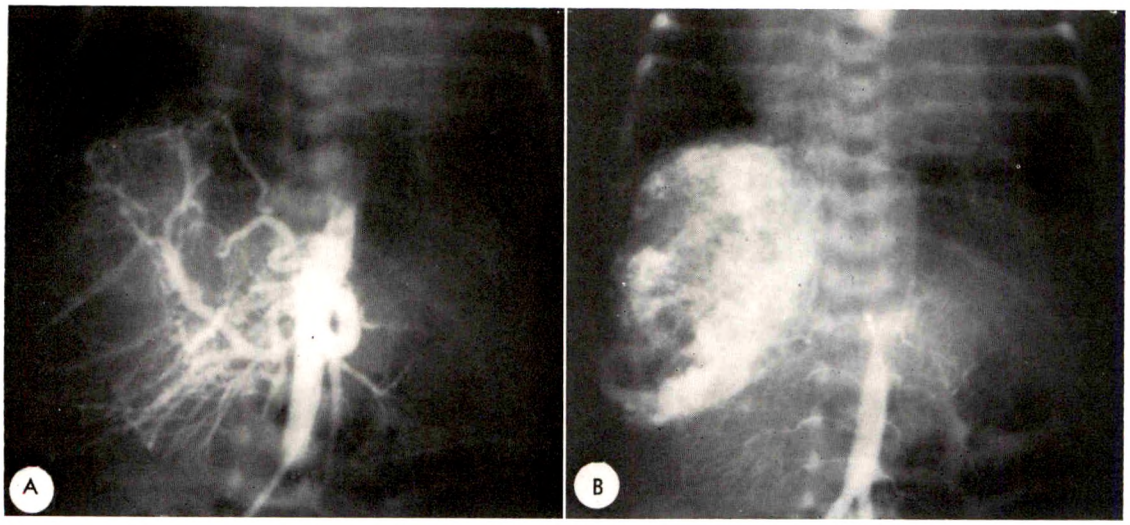


Fig. 3. (*A*) At $\frac{2}{6}$ second after injection of contrast material into the abdominal aorta a large hepatic artery is demonstrated with many enlarged vessels entering the liver. (*B*) At $1\frac{1}{6}$ seconds after injection a large angiomatous tumor of the right lobe of the liver is seen.

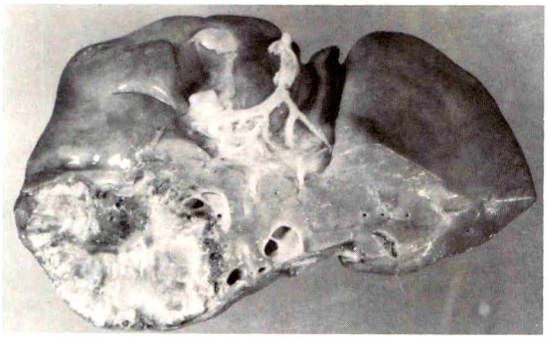


FIG. 4. Photograph of gross specimen of the liver showing the extensive tumor on the cut surface of the right lobe.

taneous regression of the neoplasm with survival may occur,[4,5,13] but hepatic lobectomy has been the advocated treatment if the liver is not diffusely involved.[4,10,14] Unfortunately the tumor frequently does involve the liver diffusely and lobectomy is not feasible.

DeLorimier and associates[5] recently described a case with cutaneous and hepatic hemangiomas in which ligation of the hepatic artery was done to relieve congestive heart failure. The hemangioma of the liver was diagnosed by abdominal aortography at 16 days of age and the hepatic artery was subsequently ligated. After this, there was considerable clinical improvement with decrease in the size of the heart and liver. The cutaneous hemangiomas continued to grow in size and number until 7 months of age, but began to involute by 14 months. Repeat angiography at that time revealed greatly reduced hepatic vascularity with the liver being supplied by branches of the left gastric and superior mesenteric arteries. The infant's growth and development were normal.

The authors point out that with conservative management of congestive heart failure only 3 of 25 patients described since 1932 have survived. Since these hemangiomas are known to regress spontaneously, treatment of cardiac failure by hepatic artery ligation may be life saving. Prompt recognition of the lesion is therefore important. In our patient the absence of cutaneous tumors was unusual and was partially responsible for the delay in diagnosis.

Hepatomegaly and cardiomegaly in an infant with congestive heart failure are expected roentgenographic findings. The calcifications within the hepatic neoplasm proved to be the diagnostic clue to the underlying pathologic process. Hepatic calcifications seen on abdominal roentgenograms have been described in older patients with cavernous hemangiomas[11,12] but have not been reported previously in infantile hemangioendothelioma. To our knowledge our case is only the second one in which abdominal aortography was performed during life. This procedure is valuable in assessing the extent of the neoplasm and in planning surgical therapy.

SUMMARY

A case of infantile hemangioendothelioma of the liver without associated cutaneous hemangiomas is reported. The infant died from high output congestive heart failure secondary to the massive arteriovenous shunting of blood through the neoplasm.

The diagnosis was established before death by the presence of hepatic calcifications and by abdominal aortography.

Early recognition of this lesion is of importance since prompt surgical therapy may be curative.

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GIANT HEMANGIOENDOTHELIOMA WITH THROMBOCYTOPENIA AND HYPOFIBRINOGENEMIA

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SINCE 1940, when the first description of capillary hemangioma with extensive purpura was published by Kasabach and Merritt,[5] at least 57 additional case histories have been recorded.[7] Most of these report patients in whom thrombocytopenia was associated with giant hemangiomata. In addition there have been 5 patients in whom giant hemangiomata were associated with hypofibrinogenemia as well as thrombocytopenia.[1]

The mechanisms for thrombocytopenia and hypofibrinogenemia have been discussed in several previous publications.[2,3,4,6,8,9] Most commonly the bleeding diathesis has been explained by platelet trapping or intravascular clotting subsequently followed by fibrinolysis.

Treatment has consisted of multiple approaches. Attempts have been made to treat the bleeding diathesis by transfusion of fresh whole blood and fibrinogen, and by administration of epsilon-amino-caproic acid, corticosteroids and anticoagulants. Surgical excision and the use of sclerosing solutions or roentgen therapy have been used to ablate the hemangiomata. When this entity was first described by Kasabach and Merritt roentgen therapy was the modality employed and it resulted in a cure of their patient.

It is the purpose of the authors to report a case of giant hemangioendothelioma with thrombocytopenia and hypofibrinogenemia treated by roentgen therapy to a successful end result.

REPORT OF A CASE

On August 31, 1966 a 17 month old male infant was admitted via the emergency room to the DeGoesbriand Memorial Hospital with a bruise on the left side of the thorax and with blood in the diapers. Three weeks prior to admission a small bruise had been noted at the base of the left chest anteriorly which disappeared spontaneously. On the evening before admission a much larger bruise appeared in the same area. No history of trauma was elicited. Blood clots were noted in the diapers just prior to bringing the child to the hospital. There was no history of epistaxis, hematemesis, melena or hematuria. There was no past history or family history of abnormal bleeding.

Physical examination revealed extensive ecchymotic areas overlying a palpable, slightly raised subcutaneous soft swelling involving the entire left anterior, lateral and posterior chest wall. There was mottling on both knees and a reticular mottling of the feet, greater on the right than the left. Petechiae were noted on the palate and in the posterior pharynx. Liver and spleen were not palpable.

The laboratory findings revealed a hemoglobin of 10.5 gm. per 100 ml.; hematocrit 33 per cent; white blood cell count 21,300 per cu. mm. with a normal differential; and a platelet count of 12,000 per cu. mm. Bone marrow by aspiration was normal. Roentgenograms of the chest and abdomen revealed a marked dorsal scoliosis of the lower thoracic and upper lumbar vertebrae.

On the third hospital day treatment was started for idiopathic thrombocytopenic purpura with prednisone. By the twelfth hospital day the platelet count had risen to 346,000 per cu. mm. The patient was discharged to continue corticosteroids in gradually reducing dosages.

He was admitted 2 weeks later because of sudden reappearance of the ecchymoses in precisely the same distribution as on the previous admission. The patient had received no steroid therapy for 1 week prior to the second admission.

Examination at this time revealed a large, flat, soft tissue mass, with overlying ecchymoses, extending over the left side of the thorax anteriorly, laterally and posteriorly. Petechiae

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were scattered over the distal lower extremities and on the hard palate. A reticular purple and red vascular mottling was noted over the right knee and upper leg. Laboratory studies on this admission revealed a hemoglobin of 9.6 gm. per 100 ml.; hematocrit of 32 per cent; and a normal leukocyte count and differential. The platelet count was 60,000 per cu. mm. A thromboplastin generation test was normal and there was no evidence of fibrinolysis.

Steroid therapy was re-started but without improvement in the platelet count or in the patient's clinical condition. During his hospital stay he bled intermittently from the nose and gums and was transfused on multiple occasions. Ecchymotic areas in the left flank fluctuated in size and color. New ecchymotic areas, which had appeared over various parts of his body, cleared during this hospitalization. On October 6, 1966 roentgenograms of the ribs revealed erosive changes involving the 8th to 12th ribs on the left, with erosion of the pedicles of some of the dorsal vertebrae. A left pleural effusion was also noted. Aortography disclosed distortion of the circulation of the left kidney and increased flow to the overlying soft tissue and into the flank region on the left. The diagnosis of neuroblastoma was entertained.

On October 14, 1966 surgical exploration of the abdomen revealed no abnormality. A left thoracentesis yielded fluid which contained no tumor cells and a surgical bone marrow biopsy was normal. Eleven days later a second abdominal exploration was performed and again no tumor was found. The spleen was removed at this time and was reported as normal. The child had an uncomplicated postoperative course but the platelet count did not rise. The fibrinogen level was found to be zero and a hematologic consultant suggested platelet sequestration or fibrin deposition and fibrinolysis as the etiology of the bleeding tendency.

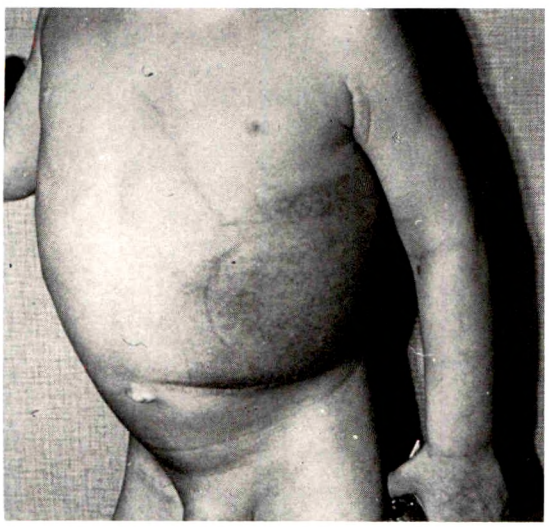


Fig. 1. Giant hemangioendothelioma with thrombocytopenia and hypofibrinogenemia. December 1966, before therapy.



Fig. 2. December 1966, before therapy.

On November 28, 1966 biopsy of the skin, subcutaneous mass, rib and muscle was performed. During this procedure there was a loss of 250 cc. of blood which was replaced. On the first postoperative day epistaxis recurred and repeated transfusions were required. On December 1, 1966 his platelet count was 20,000 per cu. mm., the fibrinogen 0.08 gm. per cent and the hematocrit 35 per cent. The biopsy showed extensive infiltration of dense ill defined endothelial cells. A diagnosis of hemangioendothelioma of the skin and soft tissue was made (Fig. 1 and 2).

The patient was referred to the Division of Radiation Therapy where the mass was treated with the following factors: 200 kv., 10 ma., added filter of 0.5 mm. copper and 1 mm. of aluminum, and a target-skin distance of 50 cm., the output being 25 r per minute. Therapy was administered through multiple 10×10 cm. tangential portals to prevent overlap of field margins, minimize the dose to the lung and kidney and yet encompass the whole of the tumor.

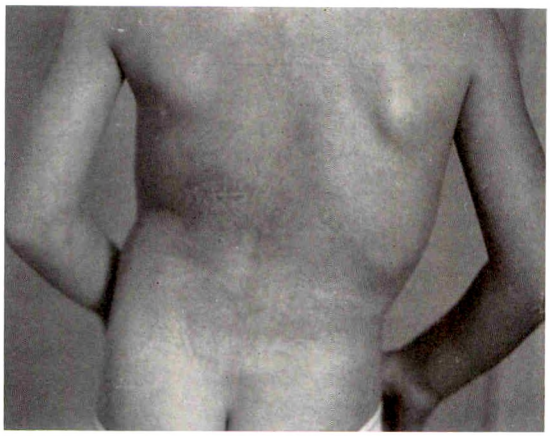


FIG. 3. October 1968, 1 year, 4 months following therapy.

From December 2, 1966 to January 10, 1967 he was given a total dose of 800 r.

By February 9, 1967 little regression of the tumor or improvement in the platelet count and fibrinogen level had been noted although no further bleeding was observed. Additional therapy from February 9, 1967 to February 23, 1967 consisted of 450 r via the same portals. A gradual increase in the platelet count and fibrinogen level with regression of the mass without new ecchymotic areas was observed.

On April 3, 1967 he was readmitted because of increasing size of the mass and recurrence of bruising about the mass for 5 days prior to admission. The platelet count was 80,000 per cu. mm. and the fibrinogen level 0.15 gm. per cent. It was decided to observe the patient for a period of time before giving any additional therapy.

The tumor mass gradually increased in size and rather alarming reductions in platelets and fibrinogen were noted. Radiation therapy was re-instituted on May 27, 1967 and completed on June 16, 1967, an additional dose of 575 r being given.

The child was followed at weekly intervals in the pediatric clinic and there was gradual diminution of the tumor and increase in platelet and fibrinogen levels. By June 30, 1967 there was no evidence of a mass and the platelet count and fibrinogen level were normal. Visits through October 1968 have revealed no evidence of recurrence of the tumor mass (Fig. 3 and 4) or bleeding manifestation. The platelet counts and fibrinogen levels have remained normal.

SUMMARY

A 17 month old child with a large subcutaneous hemangioendothelioma with platelet trapping and hypofibrinogenemia is reported.

Despite multiple transfusions, splenectomy and corticosteroid therapy there was no improvement.

Administration of roentgen therapy with a cumulative dose of 1,825 r during a time interval of 7 months resulted in complete regression of the tumor mass and return of normal platelet and fibrinogen levels.

The case demonstrates that conventional doses of roentgen therapy may have to be exceeded before the full benefit is achieved in this type of tumor.

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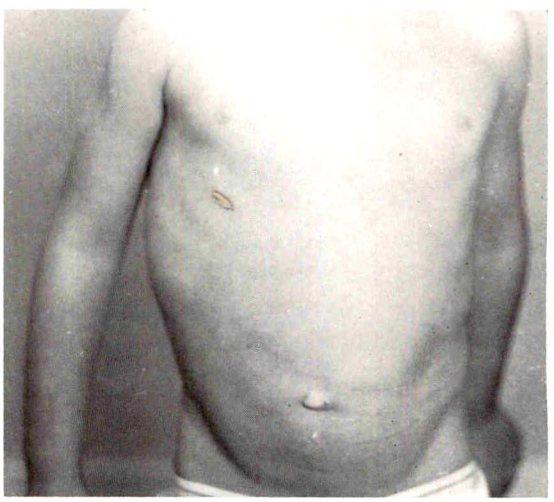


FIG. 4. October 1968, 1 year, 4 months following therapy.

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GANGLIONEUROBLASTOMA: ANGIOGRAPHIC-HISTOLOGIC CORRELATION*

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NEUROBLASTOMA and ganglioneuroblastoma constitute the second most common malignant solid tumor of childhood.[5] Little recorded data concerning the angiographic findings in these neoplasms, however, are available. McDonald and Hiller[6] described arteriographic findings in 14 cases of neuroblastoma, but state that "references to arteriographic findings . . . are scanty, the technique being virtually ignored . . . in these conditions." In their material, a pathologic tumor circulation was found in 6 cases (46 per cent) and displacement of the kidney or extrinsic distortion of its outline was present in every case. A review by Rossi[7] of angiography in adrenal tumors comprised a total of 23 cases. A single case of ganglioneuroma was included, in which angiography showed vessels in the vicinity of the tumor to be "sparse, irregular and displaced," but failed to show tumor stain. In view of the paucity of the available material in the literature, we feel it worthwhile to record this case.

REPORT OF A CASE

L.S. is a 5 year old white female who had a 1 month history of irritability, weight loss, myalgias, general malaise, and intermittent febrile episodes. The patient was referred undiagnosed to the DeGoesbriand Memorial Unit of the Medical Center Hospital of Vermont because of dropping hemoglobin and continuing fever.

The admission physical examination revealed a pale, irritable child with a 5 finger splenomegaly. Hemoglobin was 7.2 gm. per cent with 1+ Coombs. The blood smear showed nucleated red blood cells. Initial vanil mandelic acid (VMA) was 21 mg. in 24 hours (top normal 7.1 mg. in 24 hours in our laboratories). Bone marrow aspiration revealed "metastatic malignant cells, probably neuroblastoma," and erythroid hyperplasia.

The positive roentgenographic findings were limited to the abdomen. Intravenous pyelography (Fig. 1) showed an oval area of finely stippled calcification, some 3–4 cm. in largest diameter, overlying the upper right renal margin. No renal displacement, however, or other evidence of mass in the right retroperitoneum, could be found. Immediately prior to surgery, right retrograde percutaneous aortography was performed. Study of the films (Fig. 2 and 3) was made difficult due to pre-existing calcification in the right adrenal area. The gastroduodenal artery was flattened and displaced slightly to-



FIG. 1. Intravenous urogram demonstrates normal renal position and function. There is an ovoid area of irregular calcification overlying the upper pole of the right kidney.

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ward the midline; the segmental renal artery to the right upper pole was also slightly displaced by the mass. The right inferior adrenal artery was more prominent than its counterpart on the left, but no evidence of pathologic "tumor" vessels could be identified. Late roentgenograms showed a vascular blush representing the superior aspect of a normal adrenal gland but the inferior portion of the adrenal gland was replaced by calcified mass. Lack of renal involvement was confirmed on the nephrogram, and the preoperative diagnosis was "benign calcified mass . . . in or adjacent to right adrenal."

At surgery, a mass 4 cm. in diameter was found, separate from the right kidney but intimately associated with normal adrenal tissue on its superior aspect. This lesion was resected, and on microscopic examination (Fig. 4) was shown to consist of interwoven nerve fibrils, large ganglion cells, scattered foci of calcium, and occasional lymphocytes. One section showed a "small clump" of neuroblasts. The final diagnosis was ganglioneuroma with a focus of neuroblastoma.

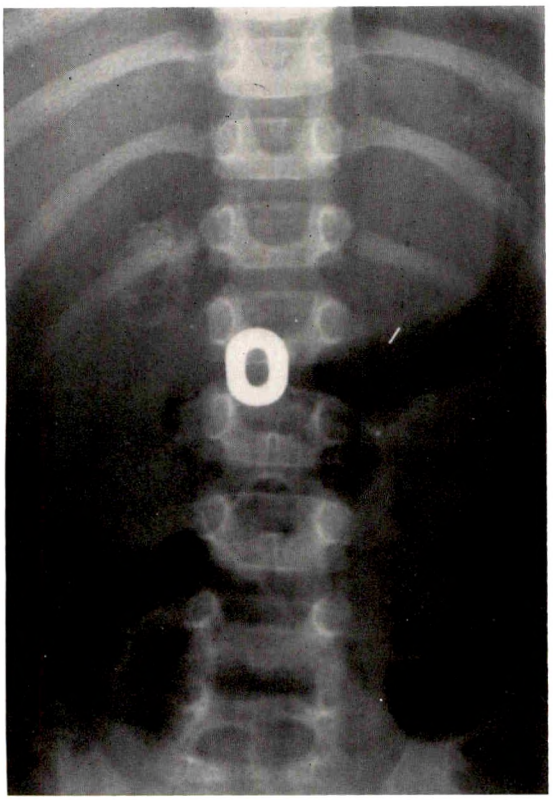


Fig. 2. Abdominal roentgenogram prior to angiography demonstrates the ovoid calcification partially obscuring the right kidney. The calcification is seen on this roentgenogram to better advantage than on the pyelogram. No bone erosion is evident. A metallic marker overlies the L1-2 interspace.

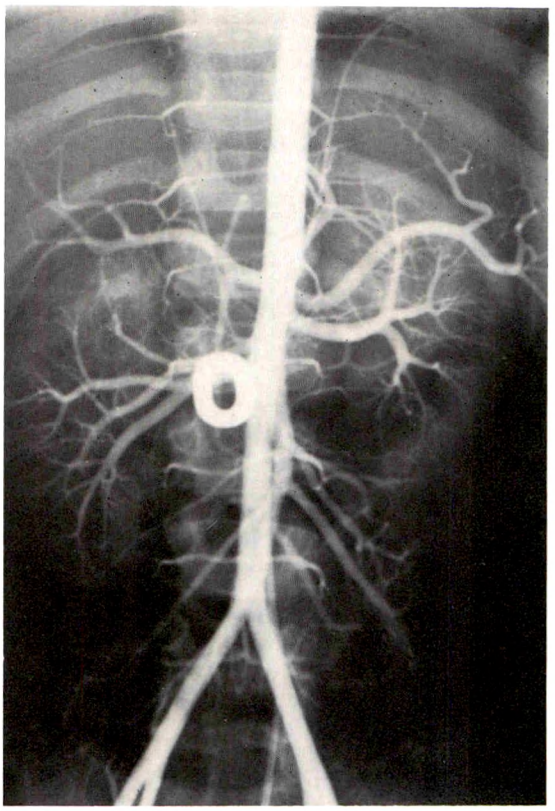


Fig. 3. Abdominal angiogram reveals straightening and slight medial displacement of the gastroduodenal artery, minimal inferior displacement of the right upper pole renal artery, and slight hypertrophy of the right inferior adrenal artery. No tumor vessels are demonstrated.

The treatment included irradiation (cobalt 60, 2,000 rads to tumor bed) and courses of vincristine, cytoxan, and prednisone, but 6 days postoperatively the VMA was 22 mg./24 hours and in 6 months the patient had persistent anemia and extremity pain.

COMMENT

Hope *et al.*[3] believe in minimal preoperative study in abdominal tumors in childhood, feeling that "repetitive" examination may increase likelihood of metastasis, and urge surgery within 24 hours. McDonald and Hiller,[6] however, propose that a 1 to 2 day delay for diagnostic evaluation is justified in neuroblastoma and related tumors. These authors further point out that aortography

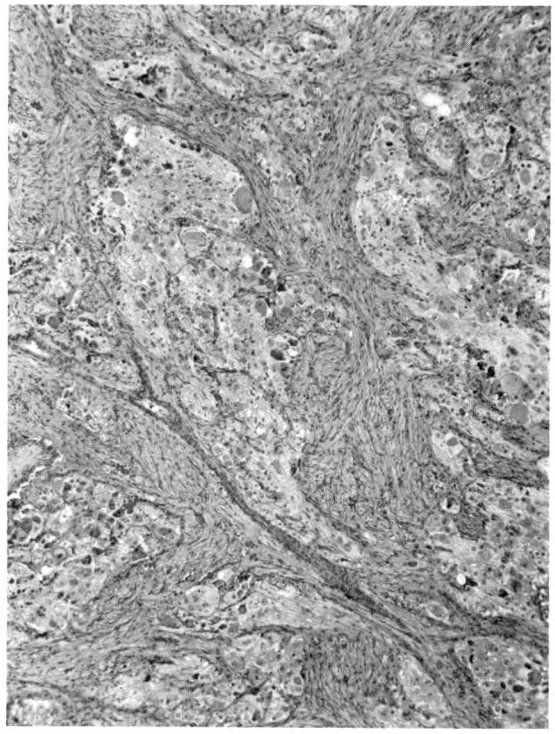


FIG. 4. Histologic study of the tumor shows mature ganglion cells throughout most of the section. There is only an occasional focus of more immature or "intermediate" neuroblasts.

may provide confirmatory evidence of the presence and nature of the tumor, aiding pyelography and cavography in predicting the site and extent of the tumor and defining its blood supply. Angiography in the case presented here gave a more accurate assessment of the size and location of the neoplasm than pyelography. Tumor stain has been a variable finding in neuroblastoma, but all such lesions of McDonald and Hiller[6] did involve the ipsilateral kidney by distortion or displacement—a finding notably absent in the case reported here.

Of additional interest in this patient is the poor correlation between the largely benign histology of the primary tumor and the more virulent behavior of the peripheral disease. However, since the report of Cushing and Wolbach[1] on apparent maturation of neuroblastoma to ganglioneuroma, the hypothesis that these tumors are different manifestations of the same disease has received general acceptance.[8] Farber[2] noted that neuroblastoma may undergo spontaneous hemorrhage and necrosis, disappear without treatment, or undergo maturation into benign ganglioneuroma. Kincaid *et al.*[4] allude to "several" cases of neuroblastoma regressing to ganglioneuroma.

SUMMARY

Ganglioneuroblastoma in a 5 year old girl was investigated angiographically.

Absence of pathologic circulation and lack of renal involvement favored a benign tumor diagnosis.

While good correlation between the overall radiologic-pathologic findings was demonstrated, small foci of maligant cells resulted in disseminated disease.

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DIVERTICULUM OF PROSTATIC URETHRA DEVELOPING POSTOPERATIVELY FROM STUMP OF CONGENITAL RECTOURETHRAL FISTULA*

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THE purpose of this paper is to present 3 case reports of an unusual type of diverticulum of the male posterior urethra. The outpouching, observed in 3 children previously operated on for imperforate anus and rectourethral fistula, was apparently caused by failure of obliteration, and subsequent enlargement, of the residual stump of the fistula. To our knowledge this finding has not been previously recorded in the radiologic literature.

REPORT OF CASES

CASE I. M.S.S., a white male, was born with an imperforate anus which was corrected during his second day of life in another institution by a combined abdominal perineal procedure. A fistula connecting the rectum with the midposterior urethra was identified, ligated and transected. For the first 3 years postoperatively the patient did well except for constipation, which required almost daily enemas. At 3 years of age he developed recurrent urinary tract infections for which he received antibiotic therapy, intermittently, for 1 year.

At 4 years of age he was referred to this hospital because of pain on micturition of a few months' duration. In the hospital it was noted that he was constipated and had some urinary incontinence. The rectum was found to be narrow but with normal sphincter control. The rest of the physical examination was not remarkable.

Urinalyses showed persistent pyuria, with abundant bacterial growth on several occasions. Roentgenograms of the abdomen and pelvis revealed no abnormalities in the bones or soft tissues. The upper urinary tract was normal on excretory urography. A combined voiding cystourethrographic and barium enema examination (Fig. 1, *A-D*) showed the following abnormalities: The rectum and distal sigmoid were rather narrow with moderate dilatation of the colon proximally. An additional short circumferential stricture formation was present at the anorectal junction. The rectum was displaced forward and to the right of the bladder by a presacral cystic mass 3×4 cm. in diameter, which communicated by a narrow neck with the midposterior urethra. The posterior urethra was dilated down to the level of the external sphincter, where there was a constant area of narrowing interpreted as a spasm of this muscle. No stricture was found at this level at urethroscopy.

Through a combined abdominal perineal procedure, the narrow segment of the distal colon was resected and the proximal colon was re-anastomosed to the anus. The presacral cystic mass was removed through a subsacral approach. At operation it was noted that the cyst narrowed to a very small fistulous tract which entered the urethra immediately below the prostate. Histologically, the wall of the cyst was composed of an external muscular coat with marked fibrosis, and of an internal layer of a normal colonic mucosa. Postoperatively, there was a prompt improvement in the constipation, but only a mild improvement in the other symptoms.

CASE II. D.B.P., a white male, was born with an imperforate anus which was corrected by a combined abdominal perineal procedure in his second day of life, at another institution. A fistula connecting the rectum with the posterior urethra was identified, ligated and transected. For the first 3 years postoperatively the patient did well except for constipation requiring almost daily enemas.

At 3 years of age he was referred to this hospital because of dribbling of urine of a few weeks' duration. In the hospital he was observed to pass small volumes of urine every 10 to 15 minutes. Physical examination was not remarkable except for an enlarged anus with

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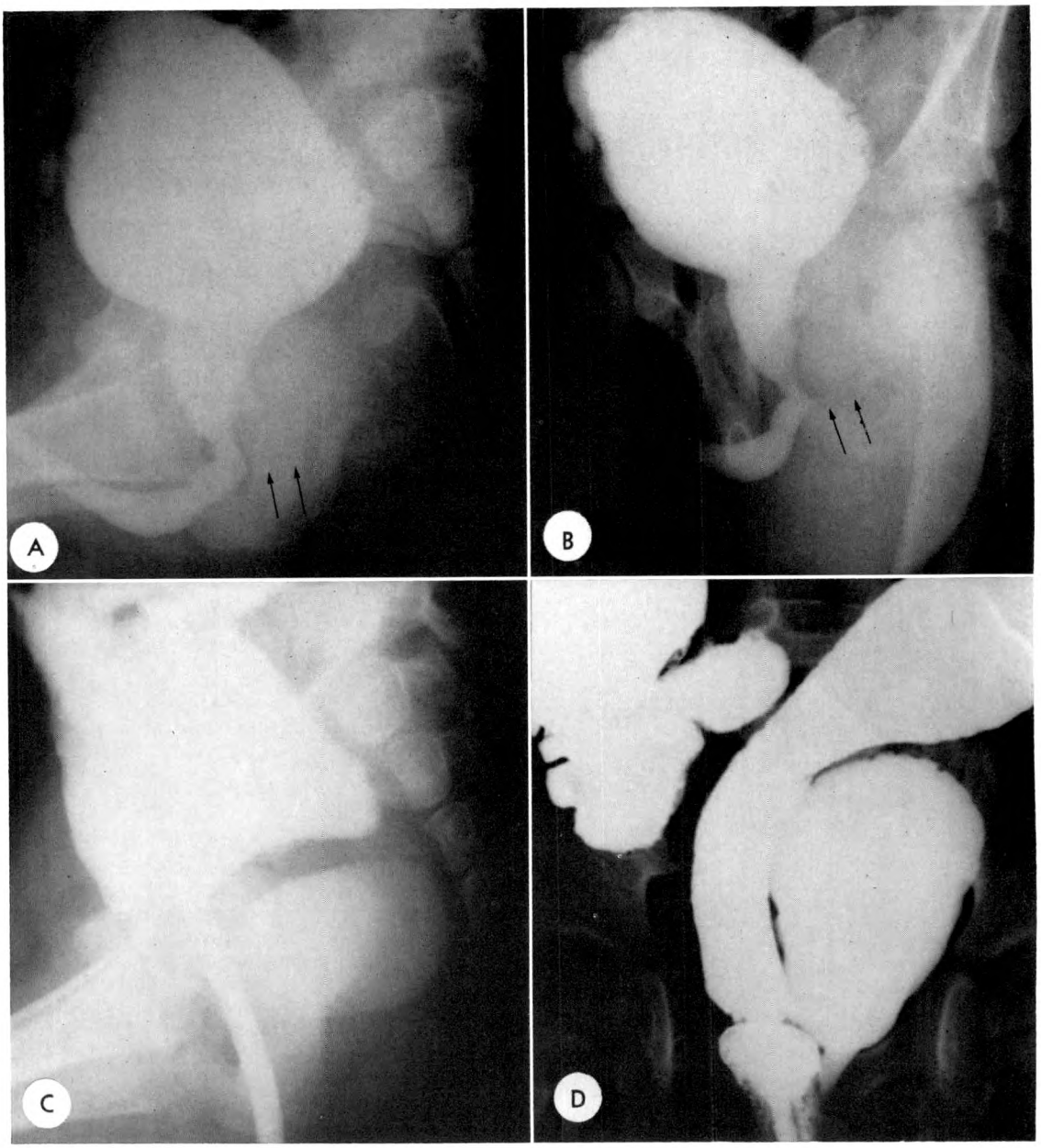


Fig. 1. Case 1. Voiding cystourethrograms and barium enema. (*A* and *B*) Presacral cystic mass communicates with posterior urethra through narrow neck (arrows). (*C* and *D*) Mass displaces rectum anteriorly and to right of bladder. Note stenosis of rectum in *D*.

protruding mucosa and a mild chordee which had been present since birth.

Roentgenograms of the lumbosacral spine showed no bone or soft tissue abnormalities. Excretory urography revealed slight bilateral ureterectasis. Voiding cystourethrography (Fig. 2, *A*, *B* and *C*) showed a large smooth-walled bladder, and mild vesicoureteral reflux on the left. The patient voided with difficulty and failed to empty his bladder completely. The bladder neck and urethra were normal, except for severe intermittent spasm of the external sphincter. In addition to these findings, the voiding study revealed a bicornuate pouch located behind the proximal urethra communicating with the midposterior urethra by a nar-

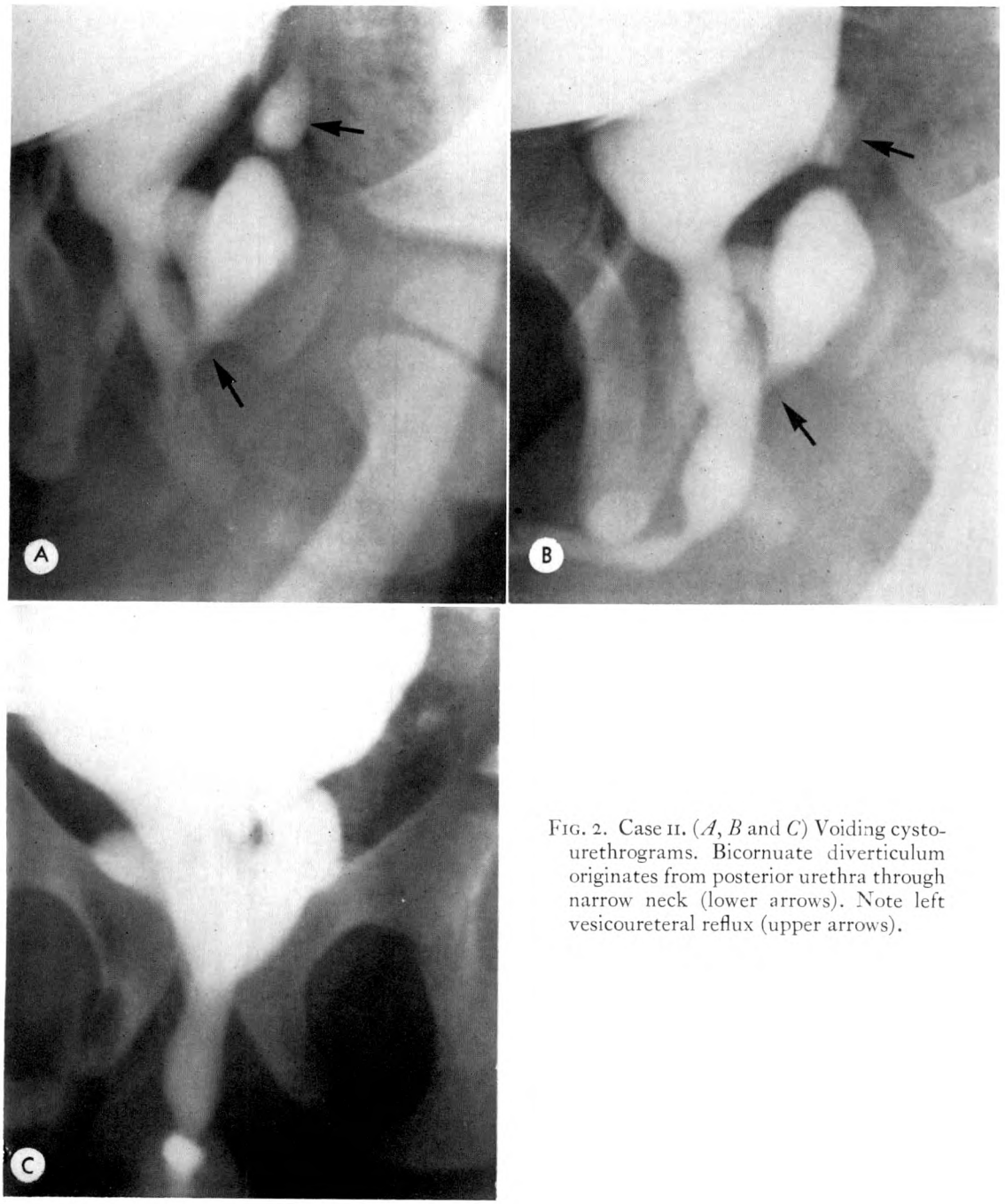


Fig. 2. Case 11. (*A*, *B* and *C*) Voiding cystourethrograms. Bicornuate diverticulum originates from posterior urethra through narrow neck (lower arrows). Note left vesicoureteral reflux (upper arrows).

row channel. At urethroscopy the opening of this cystic structure was seen to be located immediately below the verumontanum. An area of apparent narrowing to the passage of the instrument was felt to be present in the distal segment of the posterior urethra.

Several urethral dilatations under general anesthesia were carried out in the following 4 months, initially for the suggested narrowing in the posterior urethra, and subsequently for a stricture in the bulbar urethra, which developed apparently as a complication of these instrumentations. During these 4 months, the patient continued to be constipated and to have

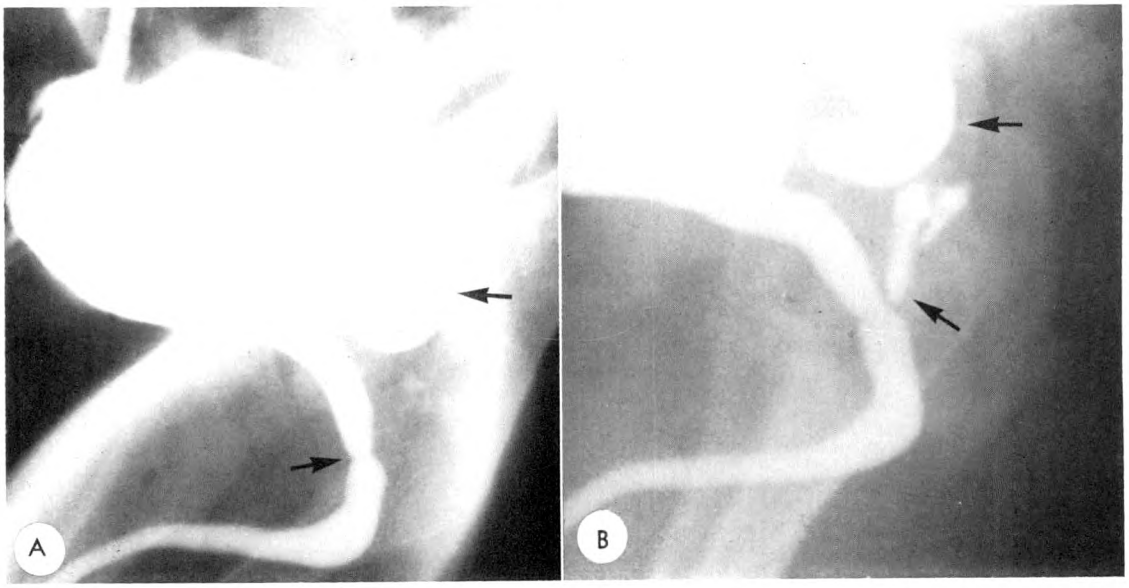


Fig. 3. Case III. (*A* and *B*) Voiding cystourethrograms. Bicornuate diverticulum originates from posterior urethra through narrow neck (*B*, lower arrow). Note urethral membrane stenosis immediately below origin of diverticulum (*A*, lower arrow), and left vesicoureteral reflux (upper arrows).

frequent urination and repeated urinary tract infections.

A re-evaluation 5 months after the first admission showed marked improvement in the stricture of the bulbar urethra, but no change in the other clinical or roentgenographic findings. The urethral diverticulum was considered as an actual or potential source of infection and was removed during the same admission through a presacral approach. At operation a pear-shaped cystic mass, measuring 3×3 cm. in diameter, was found behind the prostatic urethra. It was connected through a small duct with the urethra at the lower border of the prostate. The connection was ligated and transected and the entire mass was shelled out without difficulty. Histologically, the wall of the cyst consisted of an external muscular coat containing some prostatic tissue in one area, and of an internal layer of typical rectal mucosa with changes of chronic inflammation. The operation resulted in a definite improvement in the urinary infections, but had little effect on the urinary frequency which was finally interpreted as a manifestation of mild neurogenic bladder disease.

Case III. J.T.P., a Latin American male, was referred to this hospital at 1 day of age because of an imperforate anus. The rest of the physical examination was within normal limits. Roentgenograms of the spine showed a malformed sacrum and several minor anomalies in some of the ribs and in some of the dorsal and lumbar vertebrae. Excretory urography revealed a dilated left pelvocalyceal system and ureter, with a normal right upper tract and bladder. Voiding cystourethrography demonstrated gross vesicoureteral reflux on the left, an iris membrane obstruction in the midposterior urethra, and a rectourethral fistula entering the posterior urethra at or immediately above this iris membrane.

The anorectal malformation was corrected the following day by a combined abdominal perineal procedure. The rectourethral fistula was ligated and transected. Postoperatively, the patient developed a severe urinary tract infection which persisted in spite of protracted chemotherapy. A Foley catheter was inserted in the bladder suprapubically during the seventh week of life with only a temporary improvement. Fever and pyuria recurred and the patient was readmitted to the hospital at 3 months of age.

Repeat cystourethrography (Fig. 3, *A* and *B*) showed bilateral reflux. The urethral stenosis was again demonstrated. In addition to these findings, the study revealed a fistulous structure originating from the midposterior

urethra. This structure seemed to bifurcate posteriorly into two short laterally placed branches.

A week later a left ureteral reimplantation was carried out, together with dilatation of the posterior urethral stenosis. At the same time, the fistulous structure between the rectum and the posterior urethra was identified and removed. Histologically, this structure was composed of an external muscular coat and of an internal layer containing both urogenic and colonic epithelium. Postoperatively, urinary tract infections continued, but were much less frequent.

SUMMARY

Three male children are reported with similar histories and clinical findings. They were born with imperforate anus which was corrected in the newborn period by a combined abdominal perineal pull-through procedure, plus ligation and transection of a fistula connecting the rectum with the mid-posterior urethra. Postoperatively, they were found to have a cyst-like structure behind the prostate which communicated through a narrow neck with the mid-posterior urethra. Histologically, the wall of the pouch was composed mainly of a muscular coat which was lined internally by rectal mucosa in 2 patients and by rectal and urogenic mucosa in the other patient.

Because of their anatomic relationship and microscopic features, these cystic structures are thought to represent the stumps of the original rectourethral fistulae which have failed to obliterate and then progressively enlarged. The failure of obliteration and subsequent enlargement of these fistulous stumps were probably precipitated by the more distal urethral obstruction, organic in one patient, functional in the other two. An additional factor which may be incriminated, but which cannot be substantiated in view of incomplete data available on the original surgical procedure, is that too long a fistulous tract was left behind at the time of the surgical correction of the imperforate anus.

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MULTIPLE PURPOSE HEAD HOLDER*

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THE need for a practical and simple head holder is ever present in the Radiology Department.

CONSTRUCTION OF A MULTIPLE PURPOSE HEAD HOLDER

We have constructed a head holder which can be used conveniently in roentgenographic exposures, verification roentgenograms for radium implant patients, and isotope brain scanning. The holder consists of 4 lucite walls, one of which is movable, sliding in a lateral direction (Fig. 1). The movement of the sliding wall can be adjusted and fastened by a pair of thumb screws. The internal maximal dimensions of the holder are 24×30×32 cm., and the width of the holder can be brought down to a minimum of 11 cm. The movable wall is provided with a slit to accommodate a 10 ×12 inch grid cassette for lateral exposures. The base has a similar device for vertical exposures. The inner wall of the movable part is 1/16 inch lucite to permit closer contact between the head of the patient and the film thus avoiding attenuation of the beam. At the base of the holder a rubber compound is attached to avoid slipping of the holder along the usually slippery roentgenographic table.

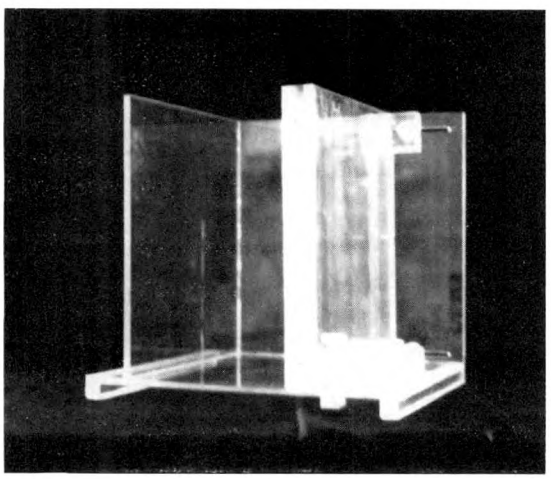


FIG. 1. View of the holder.

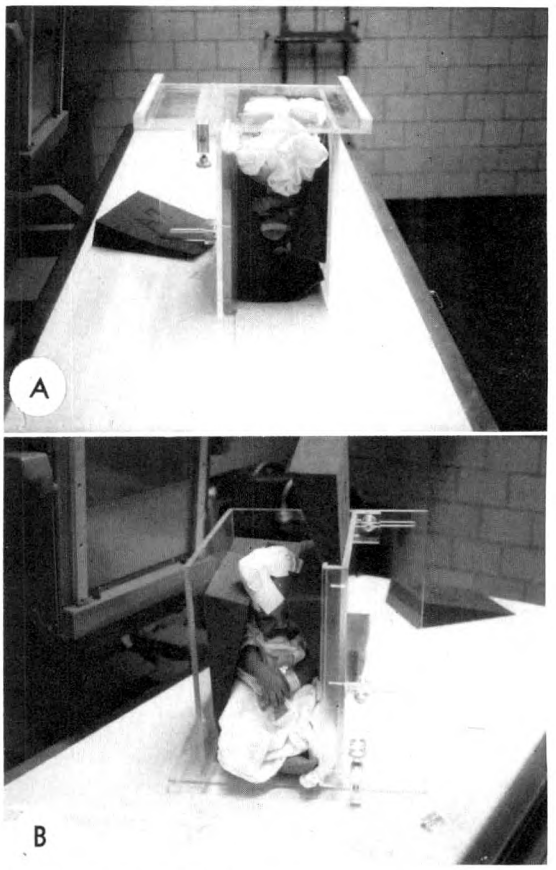


FIG. 2. (*A* and *B*) Infant immobilized within the holder placed in the desired direction of the roentgen-ray beam.

USEFULNESS OF THE MULTIPLE PURPOSE HEAD HOLDER

There are 3 different uses for the multiple purpose head holder which we have tried out in our daily work.

(1) In roentgenography, the device, aided by proper rubber sponges, permits easy immobilization of the head of an uncooperative or unconscious patient. It can also be used for immobilization of infants and children; the presence of transparent ma-

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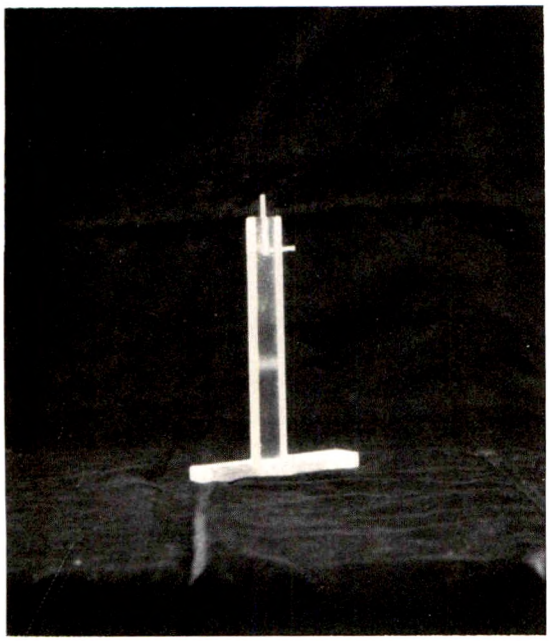


Fig. 3. Beam angulation device.

terial has a better effect on the children than the sometimes used closed wooden boxes. An interesting additional benefit was obtained when unusual positioning of an infant was required. The infant was completely immobilized within the lucite holder and the whole system could be easily placed and maintained in any desired direction of the diagnostic beam (Fig. 2, *A* and *B*).

(2) We feel that this device has an important application in taking verification roentgenograms following interstitial implantation of radium needles, or other radioactive material in the lower facial region (tongue, tonsils, etc.). Two exactly perpendicular roentgenograms of the implant are needed for reproduction of the implant in order to calculate the dose distribution throughout the implanted area. This is accomplished by placing a beam angulation device in the center of the irradiated field (Fig. 3). Figure 4 clearly shows the differences between the proper and non-proper alignment of the perpendicular fields.

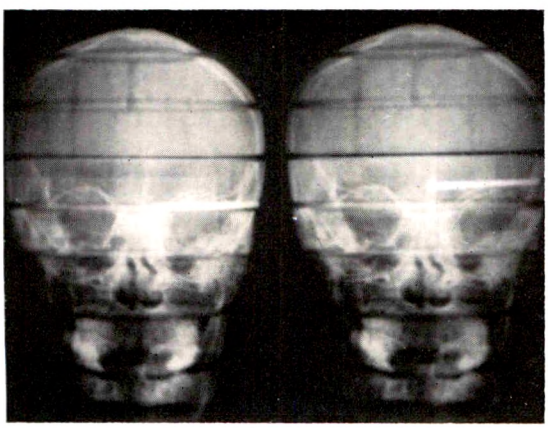


Fig. 4. Proper and non-proper alignment of perpendicular fields on head phantom.



Fig. 5. Immobilization of the patient for brain tumor scanning using a Picker Dynapix machine.

(3) Finally, the holder can be used successfully in immobilizing the head of the patient for brain scanning. Figure 5 illustrates a patient scanned for a brain tumor localized with Tc^{99m}, using a Picker Dynapix machine. The patient, fitted within the holder with the aid of rubber sponges, can complete comfortably the entire scanning procedures.

CONCLUSION

The multiple purpose holder is simple and can be constructed in one's departmental workshop.

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AUTOMATIC VIEW BOX

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THE problem of collimation of the roentgen-ray beam has been solved for many years by a multiplicity of devices, but the problem of automatic light collimation on the standard 14×17 inch view box has, to our knowledge, not successfully been accomplished. Light collimation about the edges of a small film placed on a 14×17 inch box has been done manually by various combinations of shuttering devices, but the automatic electric view box has not heretofore been available for commercial market and in standard view box size. We have now successfully developed such a view box which shows in the accompanying illustrations its ability to collimate the light.

The unit (Fig. 1) is just 1 inch thicker

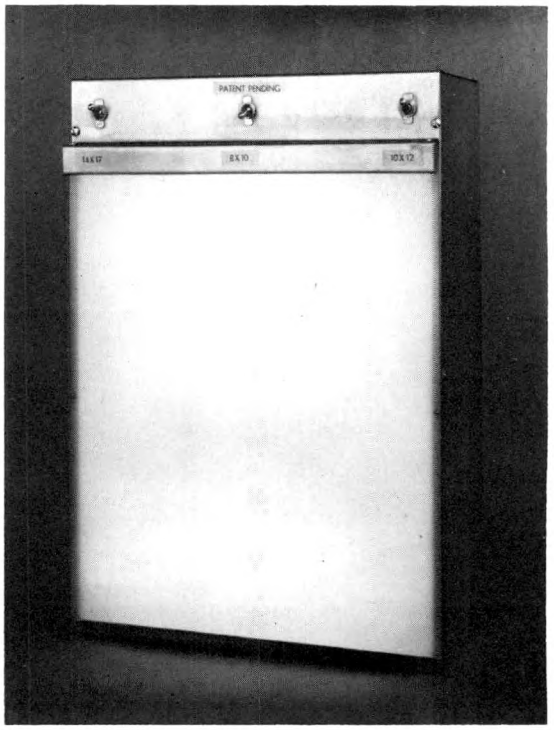


FIG. 1. View box.

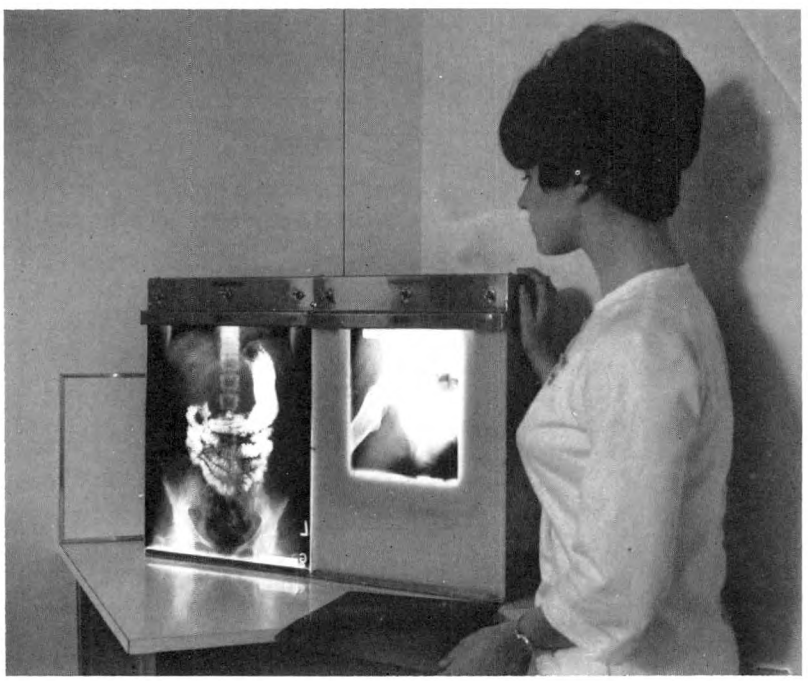


FIG. 2. Collimated to 8×10 inch size.

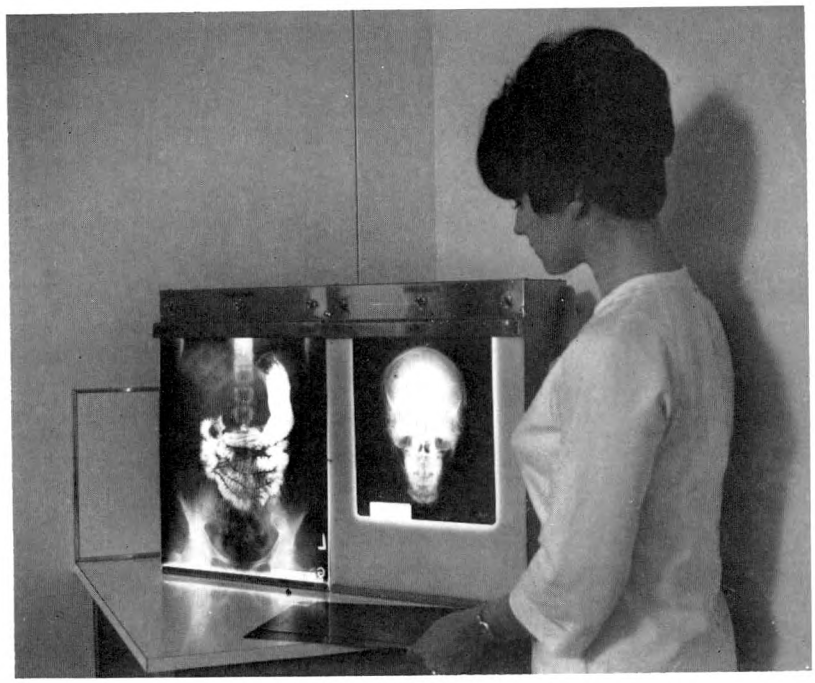


Fig. 3. Collimated to 10×12 inch size.

than the standard view box of the same over-all size, and is wholly automatic. When it is initially turned on, an 8×10 inch sharply collimated viewing area is all that is seen (Fig. 2). If, in subsequent steps, a 10×12 inch film is placed on the view box, an instant 10×12 inch collimated light aperture (Fig. 3) is formed, and similarly, if a 14×17 inch film is placed on the view box, the standard 14×17 inch aperture (Fig. 4) returns. No manual triggering or switching is necessary; the

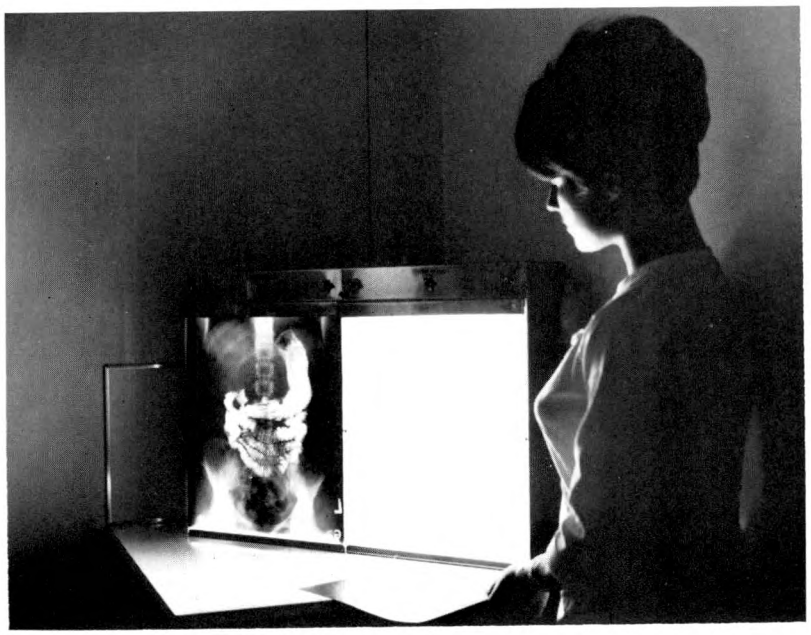


Fig. 4. Standard 14×17 inch size.

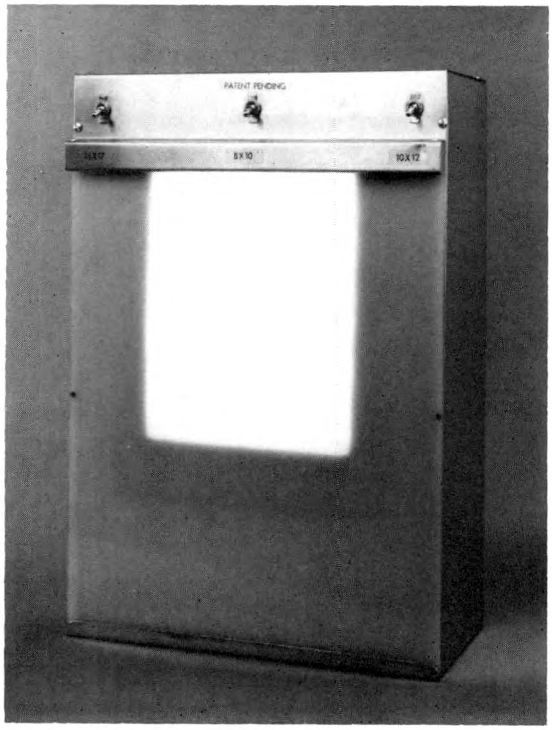


FIG. 5. Automatic return to 8×10 inch size.

view box senses the size of the film and instantly shutters to that size. When either the 14×17 inch or the 10×12 inch film is removed, the view box instantly collimates back to the standard 8×10 inch size (Fig. 5). When desired, electric switches will allow a hold of the 10×12 inch collimation, or a hold of the 14×17 inch collimation, or a return to automatic cycling.

The unit uses a cold cathode tube rather than the standard fluorescent lights, thus having at least 5 times the life of fluorescent lights. The unit comes singly or in banks of 2, 3 and 4 and is commercially produced by an x-ray accessories manufacturer.*

We have found that it is a most valuable aid in relieving eye-strain and even more valuable in increasing visual acuity at the periphery of the films.

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* Cascade X-ray, P.O. Box 73, Yakima, Washington.

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EDITORIAL

PEDIATRIC RADIOLOGY—ITS RELATIONSHIP TO GENERAL RADIOLOGY

IT IS apparent that as pediatrics has developed as a specialty dealing solely with the normal growth and development of the infant and child as well as the diseases peculiar to this age group, so too is pediatric radiology emerging as a specialty in its own right. Pediatric radiology is in essence general radiology but concerned with the problems of an age group rather than a subspecialty relating to a specific organ or organ system. As such it is as broad in its scope as radiology of the adult patient.

The Society for Pediatric Radiology was founded 11 years ago and represents one of the steps in its evolution. The Society has served both as a scientific forum and as a forum for the discussion of such questions as the nature of, and length of, training for pediatric radiology and the necessity for or desirability of certification in this specialty.

The problems in the evolution of pediatric radiology have been similar to those that have been encountered in the evolution of adult radiology. The development, particularly in academic institutions, of radiation therapy, nuclear medicine, angiography, neuroradiology, and more recently, ultrasonics and thermography has been achieved in Departments of Radiology primarily oriented to the adult patient and are now finding application in Departments of Radiology oriented to the needs of children. The impetus for such development has arisen in response to clinical demands in most instances, the demands of teaching and research in others. Departments of Pediatric Radiology must be able to provide the same specialized services established in many general radiology departments and in nearly all such departments in academic institutions. Diseases unique to childhood often require modification of techniques commonly applied in the study of the adult with similar problems. In the pediatric patient, the vessels are smaller, the heart rate more rapid, the blood loss more critical and the congenital anomalies more frequently encountered.

Most pediatric departments and hospitals are relatively small compared to the adult counterparts with which most are associated, but they have all of the clinical, teaching and research responsibilities of the units devoted to the care of adults. Is it possible that the Departments of Pediatric Radiology are able to provide subspecialists with sufficient patients, equipment and monetary support? In a few of the larger pediatric hospitals the answer is affirmative but for many, no. The immediate solution for the smaller pediatric hospitals then may well be dependent upon the degree to which the pediatric radiologist develops a working relationship with the adult unit. This association must be such that under the aegis of the pediatric radiologist there is sharing and maximal utilization within specific areas of personnel and in some situations space and equipment. This must be done in such a way that the pediatric patient is not lost to the pediatrician or to the pediatric radiologist but rather benefits from the knowledge of the adult subspecialists and their techniques. Communication between the subspecialists in adult radiology and the pediatric radiologist will be the basis for such cooperation and will make it feasible and mutually beneficial. The future development of pediatric radiologic subspecial-

ties may well stem from such relationships inasmuch as the current evolutionary trend in pediatric hospital practice appears to be towards the consolidation of small pediatric units in the community hospitals into larger units within pediatric hospitals.

These areas of mutual concern have to do with training programs, in general, diagnostic radiology as well as those in pediatric radiology. There would seem to be little doubt but that training in the two areas will be dependent upon close affiliation and integration of the specialties.

In addition, interest of the pediatrician in the fetus and in longitudinal studies of disease unites him with the radiologist, obstetrician and other specialists in a common effort. The joint follow-up of healthy and ill children into adult life offers opportunities to learn how diseases of the adult may have their beginnings in the infant and child. Such cooperation and mutual concern will strengthen both pediatric radiology and adult radiology.

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Philadelphia, Pennsylvania 19133

NEWS ITEMS

AMERICAN SOCIETY OF THERAPEUTIC RADIOLOGISTS

Announcement of Placement Bureau

The American Society of Therapeutic Radiologists has established a Placement Bureau for therapeutic radiologists at the Medical College of Virginia in Richmond. The function of this Bureau will be to make contacts between therapeutic radiologists seeking new positions and institutions or groups of radiologists who are seeking the services of a therapeutic radiologist. Information received from the therapeutic radiologists will remain confidential.

The institutions or radiologists seeking a therapeutic radiologist will be required to complete a questionnaire which will list among other things socioeconomic aspects of the position, available space and equipment, available technical help, work load, and prospective plans for expansion or increasing patient care facilities. Upon request by therapeutic radiologists, the above information will be forwarded at routine intervals to those seeking a new position.

Anyone desiring additional information as to this Placement Bureau may obtain same by contacting E. Richard King, M.D., Director of the Placement Bureau, American Society of Therapeutic Radiologists, Box 131, 1200 East Broad Street, Richmond, Virginia 23219.

SEVENTH NATIONAL BIOMEDICAL SCIENCES INSTRUMENTATION SYMPOSIUM

Imagery in Medicine

The 1969 Biomedical Sciences Instrumentation Symposium (BSIS) sponsored jointly by the Biomedical Sciences Division of the ISA and the University of Michigan and coinciding with the 100th Anniversary of the University Hospital will have as a theme, "Imagery in Medicine." It will be held at the Chrysler Center, The University of Michigan, Ann Arbor, Michigan, May 19–22, 1969.

Recent advances in theory and development of related medical instrumentation will be presented. A total of 51 papers have been programmed during the 4 days.

The sessions are: Economics of medical products; new developments; holography; neutron radiography; medical television and teaching aids; image processing; computer graphics; and radionuclide imaging.

Industrial exhibits are also planned.

Address inquiries for registration, housing, and other information to: 1969 BSIS, c/o Ernest E. Sellers, Host Chairman, Box 618, Ann Arbor, Michigan 48107.

RADIATION RESEARCH SOCIETY

The Radiation Research Society announces the appointment of Marsh Tours, Inc. of New York as the Society's Official Travel Agency for the Fourth International Congress of Radiation Research, to be held June 28 through July 4, 1970 in Evian, France.

The objective of this appointment is to assist Society Members in obtaining the best of possible rates for travel to the International Congress. Through the coordination efforts of Marsh Tours, the most conducive group travel arrangements may be made for members who wish to participate.

For further information please contact Richard J. Burk, Jr., Executive Secretary, The American University, Washington, D. C. 20016.

The address of Marsh Tours, Inc. is 630 Fifth Avenue, Rockefeller Center, New York, New York 10020.

ROYAL SOCIETY OF EDINBURGH

David Anderson-Berry Prize (1969)

A David Anderson-Berry Silver-Gilt Medal, together with a sum of money amounting to not less than one hundred pounds sterling (£100/US $240), will be awarded by the Council of the Royal Society of Edinburgh during 1969.

The prize will be awarded for recent

work on the effects of X rays and other forms of radiation on living tissues. Published work will be taken into consideration if submitted to the Society with the application.

In addition to direct application for the prize, proposals may be made on behalf of others.

Applications and proposals must be in the hands of the General Secretary, Royal Society of Edinburgh, 22/24 George Street, Edinburgh 2, Scotland, *not later than June 30th, 1969.*

HARVARD UNIVERSITY

Francis A. Countway Library of Medicine

One of the nation's largest historical collections of radiologic literature and equipment, including a number of letters written and signed by Dr. Wilhelm C. Röntgen, discoverer of the X ray, was presented to the Francis A. Countway Library of Medicine at Harvard University on February 12, 1969 by Lloyd E. Hawes, M.D., of Wellesley, Massachusetts. The collection has been assembled for the past 10 years.

Dr. Hawes is radiologist at the Peter Bent Brigham Hospital and Lecturer on Radiology at the Harvard Medical School. He is also Honorary Curator of the Historical Collection in Radiology at the Countway Library and for several years has served as Historian of the New England Roentgen Ray Society.

Over 1,000 books, early X-ray catalogs, reports of eminent radiologists, including 150 autographed papers, and an extensive assembly of X-ray equipment ranging from early tubes of the late 1800s to those of recent manufacture comprise the collection.

ABSTRACTS OF RADIOLOGICAL LITERATURE

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ROENTGEN DIAGNOSIS

Genitourinary System

Anderson, R. Arteriography in polyarteritis nodosa. *Brit. J. Urol.*, Oct., 1968, *40*, 556–559. (From: Radiology Department, Royal Free Hospital, Grays Inn Road, London W.C.1, England.)

The renal arteriographic findings in polyarteritis nodosa may include arterial aneurysms, arteriovenous fistulae, hematomas and infarction. Peripheral aneurysms, which may be saccular or fusiform, are usually multiple. The aneurysms may appear as small areas of density in the capillary phase. The arteriovenous fistulae are demonstrated as pools of contrast material along the course of an artery and demonstrate early venous return from the involved segment. Intrarenal hematomas appear as space occupying lesions in the parenchyma with distortion of the renal outline and distortion and displacement of renal vessels. Distortion and apparent absence of vessels may be produced also by thrombosis with recanalization. Extravasation may be seen where hematomas are recent.

The diagnosis may be established by biopsy of muscle, nodules, or peripheral nerve. The kidney is the most rewarding site for biopsy, especially in patients presenting with clinical picture of glomerular nephritis. The glomerulitis typical of periarteritis will be seen. Certain inherent dangers are present in renal biopsy in the presence of vascular disease. Cases of arteriovenous fistula resulting from renal biopsy in periarteritis have been described in the literature and an additional such case is reported in this paper. The kidney is apparently prone to develop the malformation since the interlobar and arcuate arteries and veins run in close proximity. These malformations tend to close spontaneously within weeks or months after biopsy. Twenty-two cases of such iatrogenic A–V fistulae following biopsy have been reported in the literature.

Local or general arterial disease, mycotic aneurysms, and tumors may also produce arteriovenous aneurysms or fistulae and must be excluded in establishing the diagnosis of renal arteriography.—*Major Edward Savolaine, MC*

Skeletal System

Tilling, Gunnar and Skobowytsh, Bohdan. Disappearing bone disease, morbus Gorham: report of a case. *Acta orthop. scandinav.*, 1968, *39*, 398–406. (From: The Department of Roentgenology and Orthopaedic Surgery, Centrallasarettet, Västerås, Sweden.)

A young girl developed osteolysis of several bones of the foot, the so-called "disappearing bone disease." She had a sprained foot at the age of 3 years but no roentgenograms were obtained.

Roentgenographic study at the age of 5½ years showed concentric atrophy of 1–4 metatarsals and the phalanges of the 2nd and 3rd toes. During the next 6 years she had several spontaneous fractures, which healed with callus, but with the progressive atrophy the callus also underwent osteolysis. The disease spread to several tarsal bones, but the 5th metatarsal and the phalanges of the great toe were spared.

The alkaline phosphatase was slightly increased during the acute phases. The patient was fairly comfortable with an arch support. There were no systemic symptoms.

The 4th metatarsal was biopsied. The articular cartilage was intact and the residual bone was roughened. The adjacent tissue was gray-yellow and did not bleed. The bone was replaced by loose "partly angioma-like tissue constructed like lymph vessels." There was nonspecific granulation tissue and necrotic bone with osteoclastic bone resorption.

Histologically this process is benign and metastases have never been seen. The disease usually makes slow irregular local progress and no regeneration of vanished bone has ever been observed. About 100 cases have been recorded in the literature.—*Martha Mottram, M.D.*

Shapiro, Jules S. Ulnar drift report of a related finding. *Acta orthop. scandinav.*, 1968, *39*, 346–353. (From: The Orthopaedic Department of the Reumasaation Sairaala Heinola, Finland.)

Many theories have been advanced to explain the ulnar drift in the rheumatoid hand. Five wrists in 4 patients were examined serially with a 6–14 year follow-up.

A line was drawn along the radial cortex of the second metacarpal to intersect with a line drawn from the tip of the radial styloid through the distal ulnar margin of the radius. The obtuse angle thus formed was measured and in all cases was found to increase as the disease progressed.

An interesting series of roentgenographic reproductions are presented which show that as the obtuse angle increases, the ulnar drift of the phalanges develops. The radial deviation accompanied by a radial rotation of the wrist precedes the drift in almost all cases.—*Martha Mottram, M.D.*

RADIATION THERAPY

Nisce, Lourdes Z., and Chu, Florence C. H. Radiation therapy of brachial plexus syndrome from breast cancer. *Radiology*, Nov., 1968, *91*, 1022–1025. (From: Department of Radiation Therapy, Memorial Hospital for Cancer and Allied Diseases, New York, N.Y. 10021.)

Brachial plexus pain occurs not infrequently in

patients with malignant disease. It is due to compression or direct invasion of the nerves by tumor, causing pain and sensory and motor deficits of the upper extremity. Since there is a paucity of information regarding the treatment of this syndrome in the literature, the authors report the effects of radiation therapy in 47 cases of brachial plexus syndrome due to metastatic mammary cancer.

The anatomy of the brachial plexus is reviewed. Involvement of the plexus by cancer of the breast is usually due to large matastatic lymph nodes in the supraclavicular or axillary areas. The resulting signs and symptoms of brachial plexus syndrome are listed and related to the cases reported. All cases had positive histologic diagnosis. Of the 47 patients, 33 were classified as operable and had had mastectomies. The majority of the cases had prior irradiation and/or surgery which resulted in fibrosis, but because of positive biopsies were considered to have their symptoms due to the tumor. The onset of the brachial plexus syndrome from the original diagnosis ranged from zero to 192 months with a mean of 33 months.

The radiation treatment field included the supraclavicular and axillary area, utilizing a single anterior portal (except in cases of excessive skin changes from prior treatment). The dose to the tumor ranged from 3,000 to 5,000 rads in 3 to 5 weeks.

The results of treatment were evaluated according to pain relief and recovery of sensory and motor deficits: 25 per cent had complete relief of pain; one-half had partial relief, and the other 25 per cent had no relief. Fifteen per cent had excellent sensory and motor recovery, 32 per cent had partial response and 53 per cent had no improvement.

The results of treatment were also analyzed according to the presence or absence of pre-existing fibrosis (those without fibrosis showed considerable improvement in the statistics) and according to radiation dosage (the higher doses proved superior). An attempt was also made to correlate the duration of the brachial plexus syndrome with radiation response, but no definite pattern was found.

It was concluded that radiation therapy is an effective means of palliation for the brachial plexus syndrome that is due to metastatic carcinoma of the breast.—*Paul M. Kroening, M.D.*

Friedman, Milton, and Pearlman, Alexander W. Benign giant-cell tumor of bone: radiation dosage for each type. *Radiology*, Dec., 1968, *91*, 1151–1158. (From: Department of Radiology, University Hospital, 560 First Avenue, New York, N.Y. 10016.)

The authors have written this paper with the purpose of bringing some order out of the chaotic mass of published data and opinions concerning the role of irradiation in the treatment of benign giant cell tumor of bone.

The study was based on 57 cases (11 of the authors' own). Cases with incomplete records were deleted. A 5 year follow-up was available in two-thirds of the cases. The tumors were classified according to combined clinical and radiotherapeutic considerations, the major parameters being: (1) age (children up to 15 years, young adults up to 25 years, and adults); (2) anatomy (membranous bones, and spine); and (3) miscellaneous types.

Cases for each of the anatomic sites are reported including special attention to those arising in the jaw in children and adults, and the rare occurrences in Paget's disease. Radiation dose ranges are depicted in scatter diagrams for each category, and also tabulated individually for each site for the different age groups. Careful scrutiny of this material led to the following conclusions:

A. In general, benign giant cell tumors in children and young adults are preferably treated with irradiation because they are radiosensitive and radiocurable with safe doses, which are smaller than required for adults.
B. Central giant cell tumor of the jaw occurs mostly in children and young adults. It can be cured with doses ranging from 2,000 rads in 15 days to 3,000 rads in 30 days.
C. Giant cell tumor of long bones is preferably treated by conservative surgery. If this is not feasible, irradiation may be gainfully employed. Doses must be higher than for children and for other anatomic sites. Even with high doses, failures do occur.
D. The possibility of malignant transformation of benign giant cell tumor following irradiation is small and of the same order of magnitude as it is following surgery.
E. For most giant cell tumors of membranous bones and the spine, irradiation is the primary therapeutic modality, as surgery often is impossible.

In addition, the authors discuss some controversial facts about giant cell tumors beside radiation dosage and indications. No attempt was made to relate histologic type or degree of malignancy to radiosensitivity due to paucity of data.—*Paul M. Kroening, M.D.*

Hinton, P., and Buschke, F. Neuroblastoma in children: 42 cases. *Radiol. clin. et biol.*, 1968, *37*, 19–28. (From: The Section of Therapeutic Radiology, University of California School of Medicine, San Francisco, Calif.)

Neuroblastoma is one of the commonest forms of malignancy in childhood. It originates from the neural crest, and the most frequent site of occurrence is the adrenal medulla. It may also occur in the retroperitoneal sympathetic chain. It may dis-

seminate via hematogeneous or lymphatic route to the liver, skull and long bones.

The authors report 42 cases of neuroblastoma between 1944 and 1967. Thirty per cent of the cases were under 1 year of age at diagnosis, and 70 per cent were under 6 years of age. The prognosis is more favorable for patients under 1 year of age. The stage of the disease did not significantly alter the prognosis. The 30 month survival of patients with bone or marrow involvement or with widespread metastases did not differ from the 30 month survival of patients in whom the disease had not spread from its site of origin.

The treatment policy accepted at the University of California consists of surgical removal of the primary tumor if possible, or irradiation of the primary tumor if inoperable, followed by irradiation of those distant foci which cause symptoms that need palliation.—*Sriprayoon Prasasvinichai, M.D.*

Hazel, J., and Bouchard, J. Radiation therapy and autoimmune disease. *J. Canad. A. Radiologists*, Sept., 1968, *19*, 117–120. (From: The Department of Radiation Therapy, Royal Victoria Hospital, Montreal, Quebec, Canada.)

The authors briefly review the disease entities more recently attributed to an autoimmune process. Some of these were treated in past years on a more or less empiric basis with radiation therapy, although their true nature was not known.

Ten cases of Mikulicz's disease generally responded favorably to moderate radiation dosage (600 to 1,300 rads in 2.5 to 5 weeks). Little significant success was noted in 8 cases of myasthenia gravis unassociated with thymoma.

Radiation therapy does contribute to a logical rationale for the treatment of certain autoimmune diseases including Hashimoto's thyroiditis, autoimmune hemolytic disease and possibly others.

Seventy recipients of cadaver kidneys received local irradiation (150 rads over 48 hours, 48 hours after transplantation) for suppression of the immune response and prolongation of grafts.—*Richard J. Torpie, M.D.*

Hirohata, Tomio. Mortality from gastric cancer and other causes after medical or surgical treatment for gastric ulcer. *J. Nat. Cancer Inst.*, Oct., 1968, *41*, 895–908. (Address: Department of Public Health, Faculty of Medicine, Kyushu University, Fukuoka City, Japan.)

The purpose of the author was to determine whether there exists an increased risk of gastric cancer in patients with benign gastric ulcer. Other selected causes of death were also investigated for possible increased incidence. A long-term follow-up (8 to 18 years) search of Massachusetts death certificates of 1,928 medically and surgically treated patients with a diagnosis of benign gastric ulcer serves as the basis of this report.

Compared to computed expected numbers of deaths by cause in the general population, there were fewer deaths from arteriosclerotic heart disease, possibly due to a general lack of obesity in gastric ulcer patients.

There was no significant deviation from expected mortality due to diabetes, cerebrovascular disease, hypertensive disease, nephritis and nephrosis, and accidents.

An increased mortality was found from liver cirrhosis, suicide, pulmonary tuberculosis and gastric ulcer itself. After the first year, there was no significant difference in over-all mortality compared to the general population.

An excess of gastric cancer deaths was found, most occurring within the first 5 years after entry into the study. These were felt to be due primarily to the inclusion as benign of some cases which were really malignant—a misdiagnosis rate of 2.4 per cent. There was no increased mortality from gastric cancer 5 years and more after entry. There was, therefore, felt to be no support for a contention of malignant degeneration of benign gastric ulcer.—*Harold Weiner, M.D.*

Bowerman, Jack W., El-Mahdi, Anas M., Lott, James Stewart, and Julian, Conrad G. Radiation abortion in radiotherapy. *Radiology*, Nov., 1968, *91*, 1013–1016. (From: Department of Radiology, Division of Radiotherapy, The Johns Hopkins Hospital, Baltimore, Md. 21205.)

Two cases are reported in which radiation therapy was complicated by intrauterine pregnancy, and the different abortion responses are discussed.

The first case was a 38 year old woman with a malignant lymphoma of the ileum, mesentery, and mesenteric lymph nodes. A dose of 2,850 rads was delivered to the midplane pelvis in 4 weeks with a telecobalt 60 unit. Gestation was estimated at 16 weeks. Forty-six days after the start of radiotherapy, a macerated fetus with complete conceptus was aborted.

The second case was a 40 year old woman at 14 weeks gestation with invasive carcinoma of the cervix, International Classification Stage IB. Intracavity and contracervical cesium 137 combined with external cobalt 60 therapy was given. The total midplane pelvic dose at the estimated uterine center from both forms of therapy was 4 850 rads given in 5 weeks. Abortion did not occur during or after therapy even though no evidence of growth was noticed shortly after therapy began. Hysterotomy 5 days after completion of therapy disclosed autolyzed parts and placenta.

The discussion includes a review of the literature and several cases are cited where low dosage, less than 1,000 rads, failed to produce abortion. In 2 cases live births occurred with no apparent observable abnormality at the ages of 11 and 4 years, after irradiation had been given at 20 weeks gestation and 6 months gestation, respectively. Gestational age, quality of irradiation and quantity of irradiation are factors involved in the abortion response to irradiation.

Serial chorionic gonadotropin titers and serial urinary estriol determinations would be valuable in studying the placental and fetal responses to irradiation. The former reflect the state of trophoblastic tissue and are not a direct measure of fetal activity, but estriol determinations accurately reflect fetal viability.—*G. F. Monzingo, M.D.*

Takaoka, A., Kaneda, H., Urano, M., and Kikkawa, S. An electrocardiographic study of cardiac damage secondary to radiotherapy of malignant intrathoracic tumors. *Radiol. clin. et biol.*, 1968, *37*, 1–12. (From: The Department of Radiology, Kyoto Prefectural University of Medicine, Kyoto, Japan.)

The authors discuss the potential as well as the actual effects of radiation on the heart consequent to irradiation of intrathoracic malignancies, notably of the breast, lung and esophagus.

Forty-one patients with these lesions were studied and none of them had any previous cardiac abnormality on clinical as well as laboratory examinations.

These patients were treated by means of cobalt 60 teletherapy and had received more than 4,000 rads at 5 cm. depth to at least 30 $cm.^2$ of their cardiac area. Electrocardiograms, hematocrit, total protein, as well as serum electrolytes were examined before, during and after radiotherapy.

Of the 41 patients, 33 (80 per cent) showed abnormal electrocardiograms. The changes consisted of sinus tachycardia (50 per cent), ST depression (50 per cent), pulmonary P (10 per cent), atrial fibrillation (7 per cent) and right bundle branch block (5 per cent). Five patients showed peculiar patterns on the daily electrocardiogram and these consisted of ST wave elevation as well as prolongation of the QT interval. The latter was associated with Hegglin's syndrome which is a clinical finding of the early second cardiac sound appearing before the end of the T wave. These abnormalities were attributed to an early myocardial damage.

The authors observed 3 cases of pericarditis out of 300, but on follow-up examination at autopsy these were attributed to myxedema and direct tumor infiltration.

The conclusion is reached that cardiac damage is a real possibility and may be a strong contributory factor to the proven clinical observation that radiation therapy of left-sided lesions in the chest had worse prognosis when compared to right-sided lesions.—*Eriberto T. David, M.D.*

Van Slyck, Ellis J., and Bermudez, Gustavo A. Radiation nephritis. *Yale J. Biol. & Med.*, Dec., 1968, *41*, 243–256. (From: The Department of Medicine, Division of Hematology, Henry Ford Hospital, Detroit, Mich. 48202.)

The clinical signs of renal impairment in radiation nephritis are subtle and may be overlooked or attributed mistakenly to the patient's primary disease. Many patients die of their primary disease (usually a malignancy) before clinical evidence of nephritis occurs, inasmuch as the latent period after irradiation may be quite long.

The severe refractory anemia that accompanies radiation nephritis may contribute significantly to the patient's symptoms and unfavorably influence his survival.

One factor in the etiology of the anemia is shortened red cell survival as evidenced by isotope studies. The presence of burr cells and schistocytes in peripheral blood smears suggests the possibility of microangiopathic lesions in small renal blood vessels causing trauma to red cells.

Defective erythropoesis characterized by marrow red cell hypoplasia with sparing of granulocytes and megakaryocytic elements has been previously established in chronic renal disease. Ferrokinetic studies show impaired plasma iron turnover rate and poor utilization of iron by developing red cells. The role of active circulating erythropoietin in this disease is uncertain.

In radiation nephritis there is also consideration of damage to significant portions of hematopoietic marrow in the radiation field. Usually pancytopenia is produced.

Patho-physiologic studies have demonstrated a variability of lesions produced in radiation nephritis. Gross perirenal or capsular fibrosis frequently occurs. Three types of intrarenal damage may be observed: (1) interstitial fibrosis of the cortex with atrophy of the tubules; (2) glomerular changes with cellular proliferation, or hyaline crescent formation or total destruction by fibrosis; and (3) intralobar and intralobular arteriolar damage characterized by fibrinoid necrosis of the vessel wall, and lipid-filled histiocyte deposits in the media and intima. The difference in pathologic response does not appear dose related.

Disagreement exists as to the primary lesion in radiation nephritis. Electron microscopy studies suggest a dominant lesion in the glomerular capillary. Other studies suggest that the basic lesion exists in the endothelium of renal blood vessels and in the epithelium of the convoluted tubules.

Most clinical reports fail to draw a clear relationship between the severity of renal damage and the

dose of radiation received. The renal plasma flow appears to fall progressively after 400 rads exposure, whereas glomerular filtration rate transiently decreases initially but rises to above pre-irradiation levels after 550 to 1,625 rads and then decreases progressively after cumulative doses of 2,000 to 2,400 rads.

Four clinical types of radiation nephritis are described:

1. Acute radiation nephritis, which appears 6 months to 1 year after irradiation, is characterized by clinical features related to hypertension, congestive failure, uremia and marked anemia. A blood urea nitrogen of over 100 mg./100 ml. or pleural effusions without generalized edema during the first 3 months are poor prognostic signs.

Urinary findings include proteinuria and hyaline, epithelial or granular casts in the urinary sediment.

The blood pressure varies but is usually highest within 6 months after onset of symptoms.

A severe, refractory, normochromic, normocytic anemia is the rule in both acute and chronic radiation nephritis in the presence of azotemia.

Death is due to hypertension, cardiac failure, hypertensive seizures and renal failure. Those improving are left with evidence of chronic nephritis.

2. Chronic radiation nephritis may develop after acute radiation nephritis or may develop insidiously after 18 months to several years after irradiation. Clinical features include hypertension, proteinuria, cylindruria, anemia and impaired renal function. In most instances, hypertension and azotemia are progressive. The insidious type of onset appears to have a somewhat better ultimate prognosis.

3. In some cases the hypertension is benign and persistent hypertension and slight proteinuria are the only findings that develop. This type seems to present about 8 months after radiotherapy.

4. Late malignant hypertension may develop after any of the preceding 3 types or may appear *de novo* long after radiotherapy. Its onset is explosive and rapidly fatal.

After the onset of radiation nephritis no specific treatment appears to modify the course although removal of a unilaterally involved kidney may be curative of the hypertension. The emphasis is on prevention of radiation nephritis.

If a dose of 2,300 r or more is to be delivered over both kidneys, renal failure can be minimized by shielding one-third of the renal mass. Pre-existing renal disease, congenital renal malformations, and impairment of renal blood supply by tumor enhance the possibility of developing radiation nephritis.

Animal studies have been performed demonstrating protection against radiation effect on kidneys (such as intraperitoneal cysteamine injection and renal artery infusion with epinephrine). Further clinical experience will be necessary for evaluation of these modalities.—*Major Edward Savolaine, MC*

Brizel, Herbert E., Scott, Ralph M., Davis, Loretta T., and Jacobson, Ahren. High energy electron beam therapy for head and neck cancer. *J. Canad. A. Radiologists*, Sept., 1968, *19*, 112–116. (From: University of Louisville School of Medicine, Louisville, Ky.)

The authors describe their experience with 147 patients treated using electron beam therapy for carcinoma of the head and neck.

The main advantage of electron beam therapy is the normal tissue sparing relative to the tumor because of the inherent rapid attenuation of the dose of an electron beam, depending on its energy. Many tumors of the head and neck are ideally suited for treatment with high energy electrons in the 10 to 25 mev. range.

The treatment planning and clinical dosimetry are relatively simple, and their experience indicates that the R.B.E. of electrons corresponds to supervoltage photon irradiation and that skin reactions do not significantly preclude radical therapy to lesions in the oral cavity, oropharynx or cervical lymph nodes. However, it is still too early to assess accurately the true value of high energy electron beam therapy for head and neck cancer because the case material is still small, although immediate tumor response parallels that from photon irradiation and patient tolerance is improved.—*Sang Ho Han, M.D.*

RADIOISOTOPES

Duffy, George J., DeNardo, Gerald L., and Abington, Robert B. Origin and evolution of radioactive pulmonary emboli in man. *Radiology*, Dec., 1968, *91*, 1175–1180. (From: Division of Nuclear Medicine, Stanford Medical Center, Stanford, Calif. 94304.)

Faced with the complication of having the regulated microemboli of MAA-I^{131} distorted by aggregation into blood clots which resulted in abnormally large and delayed precapillary embolization of the lungs in 2 patients, the opportunity to study and document the results was exercised. The clinical behavior of these 3 types of "radioactive" emboli are defined: (1) MAA-I^{131} of usual particle size; (2) MAA-I^{131} incorporated in fresh clot in syringe; and (3) MAA-I^{131} incorporated in organizing clot situated in vein of forearm.

Satisfactory periods of follow-up (67 days in Case I and 46 days in Case II), and frequent, controlled measures of the ultimate fate of the unusually acquired emboli were obtained. Case II was studied post mortem, after bronchopneumonia had intervened as the terminal insult, and a single organizing embolus (0.2×0.1 cm.) containing radioactivity was identified. However, neither case demonstrated adverse clinical signs or symptoms as a result

of this unusual type of embolization. Further, *in vitro* studies were done to prove conclusively that an admixture of MAA-I^{131} and blood in a syringe formed, on standing, fresh clots that contained, gram for gram, significantly higher count rates than the unclotted blood residue.

The possibilities of improper commercial preparations or user handling prior to time of injection were satisfactorily excluded in both cases. A normal biologic half life in the lung of properly prepared and administered MAA-I^{131} of 3 to 12 hours has been established by previous investigators. It is shown that biologic half lives of 3 to 5½ days can be had when MAA-I^{131} is allowed to incorporate in fresh clots of blood in a syringe prior to injection, and that new foci of radioactive embolization can be identified at least 4 days after an injection is made into a thrombotic vessel.

This warning of the inherent hazards of injecting MAA-I^{131} into blood which has been drawn and allowed to stand, and the impropriety of injecting into thrombotic vessels should be considered by all who utilize this procedure.—*F. C. Petty, M.D.*

VINCENT, WILLIAM R., GOLDBERG, STANLEY J., and DESILETS, DONALD. Fatality immediately following rapid infusion of macroaggregates of ^{99m}Tc albumin (MAA) for lung scan. *Radiology*, Dec., 1968, *91*, 1181–1184. (From: Cardiovascular Research Unit, University of California, San Francisco, Calif. 94122.)

The authors report the first fatality and the second patient reaction known to date following the infusion of macroaggregates of albumin for a lung scan.

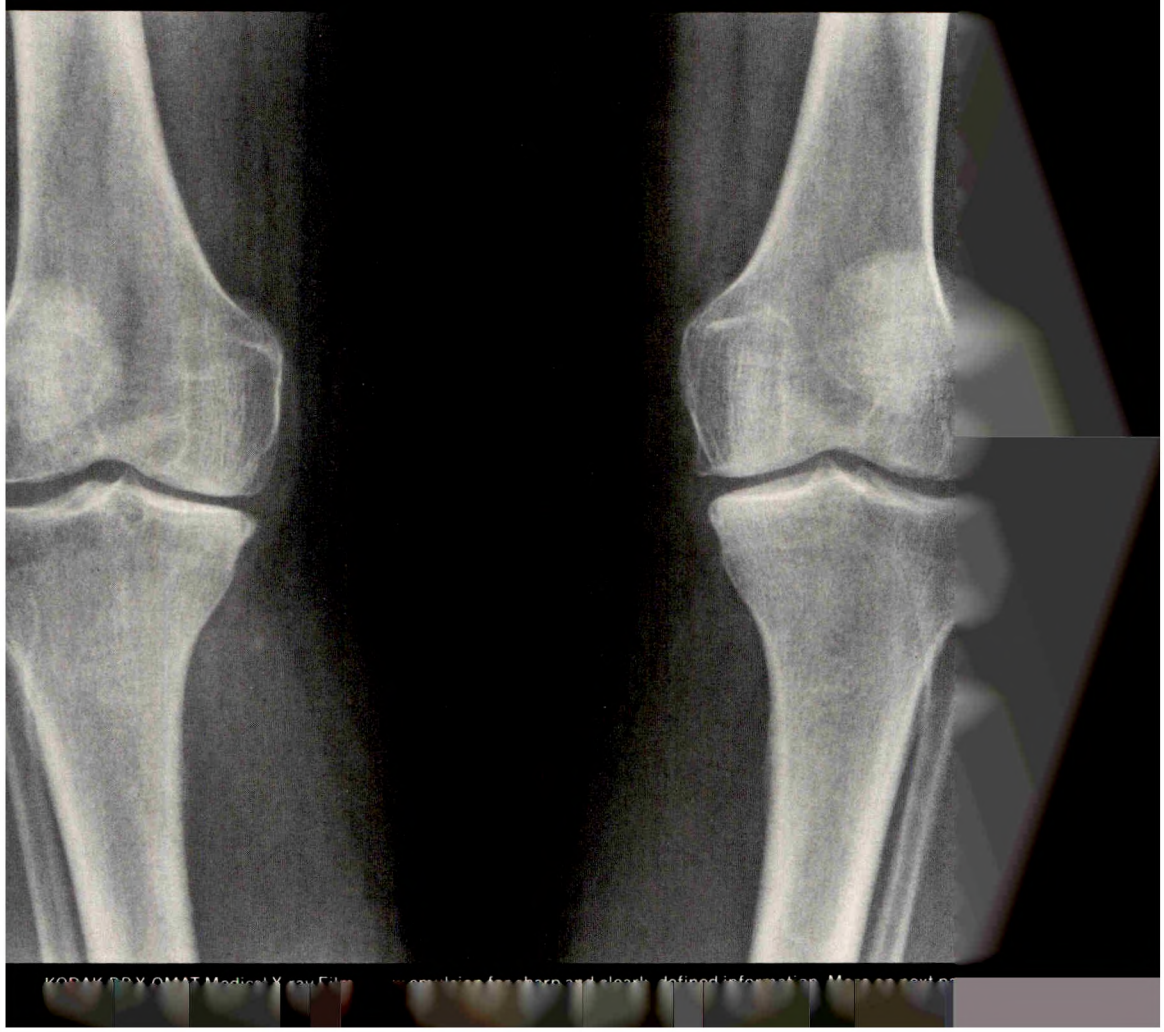
The patient was a 7 year old Caucasian male who had undergone a ventriculojugular shunt shortly after birth to alleviate noncommunicating hydrocephalus. The shunt functioned well until the child was 6½ years of age when it required revision. Fifteen months later the child developed dependent edema, with dyspnea and cough on exercise. The chest roentgenogram at that time disclosed cardiac enlargement and prominence of the pulmonary artery and the right ventricular pressure was found to be 120 mm. Hg. As a result, the intravascular portion of the shunt was revised and directed into the peritoneal cavity. During the next 5 months the symptoms increased with no benefit from therapy. A second cardiac catheterization showed a ventricular pressure of 136/20–30 mm. Hg a angiocardiography was tolerated with no adve action and no elevation in right atrial pressure weeks later a lung scan was attempted by an venous injection of a MAA suspension which tained 3.8 mg. (0.16 mg./kg.) of albumin an μc Tc^{99m} in 3.8 cc. volume. Within 1 minute t tient developed labored respiration and wh followed by apnea and unconsciousness. All at resuscitation were unsuccessful. At autopsy, was no evidence of antemortem thrombi in the cava, heart or lungs. However, the microscop amination showed medial hypertrophy of t teries and arterioles, plus marked cellular a brous thickening which was predominantly in centric fashion, suggesting embolic basis of th monary vascular disease.

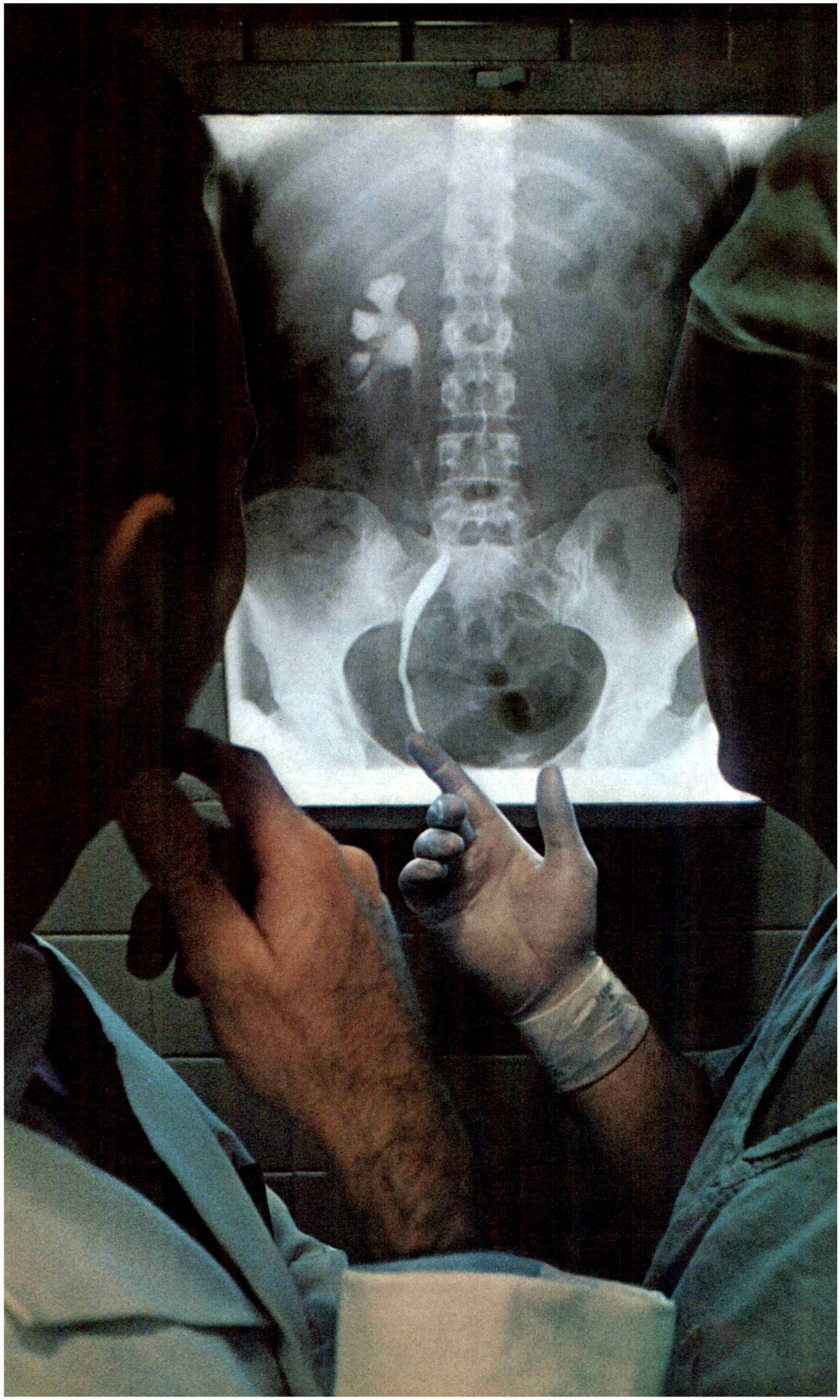
The authors discuss the various possible ca this abrupt fatal reaction including mech vascular obstruction, anaphylaxis to the parti human serum albumin, toxic pharmacologic of the ferric chloride added to the MAA suspe and coronary or cerebral effect due to intrac shunting.

Although other causes cannot be exclude tirely, in this case, it seems reasonable to fo the mechanical obstruction to the pulmonary flow as the major cause of the reaction. The particle size of this particular lot of MAA pr tion used was not determined but is usually 50 microns in the authors' laboratory. Als monary vascular disease of the type that was p in this patient is associated with a generaliz crease in arterial lumen diameter as contraste focal perfusion abnormalities in patients wit boli, infarction, inflammation, localized emph or tumors. Therefore, when general pat changes reduce the cross-section area of the p nary vessels, sudden removal of a portion of maining vessels could lead to a critical level sistance to blood flow and a prompt fatality.

The authors emphasize that lung scanning verse types of focal perfusion abnormalities is tively safe procedure as evidenced by only 1 pr report of an adverse reaction in an estimated patient scannings. However, the relatively ra tient with significantly increased risk to MAA tion should be identified by clinical signs of pulmonary hypertension.—*E. B. Best, M.D.*

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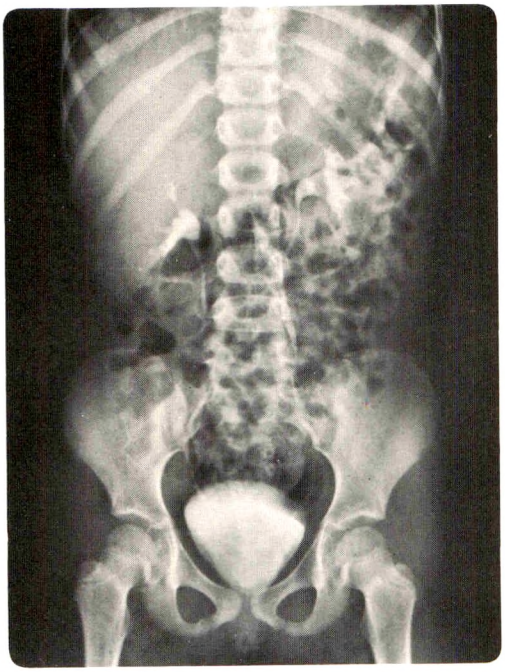
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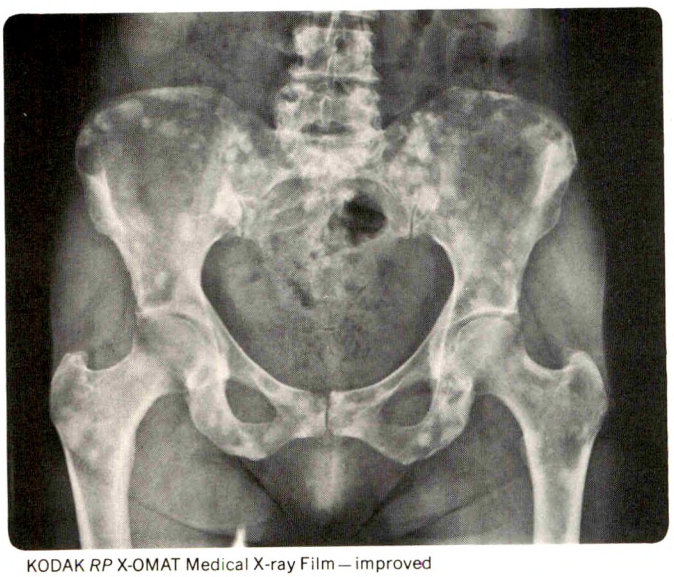
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For summary of contraindications, precautions, and side effects, see end of this advertisement.



the medium:

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Squibb Ipodate

the message:

maximum concentration... excellent toleration

high absorption index—"No one will dispute the statement that the diagnostic reliability of oral cholecystography depends upon the degree of absorption of the contrast medium employed."[2] Radioisotope studies with ipodate sodium show a markedly improved absorption index (approximately 70 per cent) with no increase in the toxic properties.[2]

excellent opacification—"In addition to its ease of administration and safety, its principal advantages are a high yield of diagnostic films...."[3]

less bowel residue—"Incomplete and variable absorption of a cholecystographic agent is not desirable, for the opacification of the gallbladder is then less dependent on the status of the gallbladder and more a reflection of the percentage absorption."[4]

"Opaque material in the bowel was found in 46 per cent of [105 patients in] the...[iopanoic acid] group as compared with 9 per cent of those [99] of the [Oragrafin Sodium Capsules]...group."[4] In another study, 49 of 100 patients receiving iopanoic acid had residue in the gastrointestinal tract, while only 15 of 100 patients receiving Oragrafin Sodium Capsules had such residue.[5]

no evidence of nephrotoxicity, infrequent side effects—In contrast to findings with other cholecystographic agents, Lewitan and Garcia[6] reported in their 246-patient study: "With ipodate calcium... there was no clinical evidence of immediate or delayed nephrotoxicity in any of the patients given it...."[6] To study possible renal toxicity, "Creatinine clearance tests were also done before and after administration of multiple doses in excess of 6 gm. in 8 cases, and showed no significant alterations."[6] However, "Multiple doses beyond 6 gm. are not recommended."[6]

In their study of 120 patients, Glenn and O'Brien reported "...no reactions in this series of patients attributable to the administration of [Oragrafin]...."[3]

And, McCrory reported that Oragrafin Sodium and Calcium was "...used routinely in cholecystographic studies in approximately 2000 patients with excellent diagnostic films and only rare and mild reactions."[7]

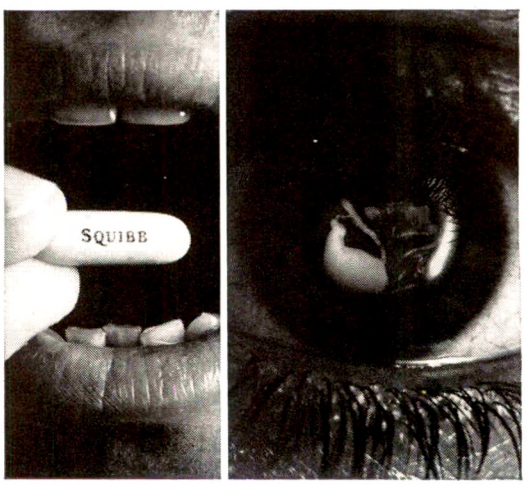
fewer side effects than iopanoic acid—According to White and Fischer,[4] 36 (36.4%) instances of side effects occurred in 99 cases with Oragrafin Sodium, 3 Gm. compared with 87 (82.9%) in 105 cases with iopanoic acid, 3 Gm. Kinds of side effects noted were nausea, vomiting, diarrhea, cramps and dysuria—all less frequent with Oragrafin Sodium (Squibb Sodium Ipodate).

Juhl,[5] in his study of 200 patients (100 on iopanoic acid and 100 on sodium ipodate), found that the incidence of nausea and vomiting was equal in the two groups.[5]

Oragrafin (Squibb Ipodate) dosage schedules
Oragrafin (calcium or sodium ipodate) permits overnight cholecystography and cholangiography.

	Gallbladder Films		Films of the Gallbladder and Biliary Ducts
11 P.M.	6 Capsules OR (or 12 Capsules)	1 packet of Granules (or 2 packets)	6 Capsules (or 1 packet of Granules, if preferred) and
next morning 8 A.M.			1 packet of Granules
9 A.M.	Visualization of gallbladder	Visualization of gallbladder	Visualization of ducts and gallbladder
10 A.M.			
11 A.M.			

For summary of contraindications, precautions, and side effects, see next page.



speed and convenience of Oragrafin® Calcium Granules

Squibb Calcium Ipodate

new clinical study[8] demonstrates improved diagnoses with calcium ipodate—"A group of 114 patients with poorly filled gallbladders after routine administration of iopanoic acid were given 6 gm. of [calcium] ipodate granules immediately following their routine cholecystography. In 66 per cent of these patients opacification of the gallbladders was obtained within 3 hours, allowing a definite diagnosis. Of the remaining 33 per cent, one-half were ultimately proven diseased." "It is apparent that many poorly visualized gallbladders can be rendered visible by the ingestion of ipodate granules.... A whole day may be saved and other diagnostic studies may be performed."[8]

patient convenience—Routine cholecystography night-before procedure is easy for patients to follow; palatable granules further enhance patient acceptability. Rapid clearance of medium permits same-day administration and gallbladder and ductal films, and if necessary, same-day re-examination; reduces need for I.V. studies.

rapid absorption permits same-day re-examination—To determine the cause of nonopacification after routine cholecystography using 6 capsules, physicians may require re-examination by repeating the procedure at a later date (sometimes doubling dose to 12 capsules), or by administering more agent the evening of the first unsuccessful examination (again sometimes doubling dose to 12 capsules), and repeating the study the next day. "The advantage of the calcium ipodate method is that the examination can be completed in five additional hours with a limited dose of contrast agent."[9]

"a valuable medium for peroral cholegraphy"[6]—Rapidly absorbed from the gastrointestinal tract, calcium ipodate has been reported by some investigators to be diagnostically superior to other oral cholangiographic contrast agents.[10,11] With careful timing of the examination and the use of tomograms or laminograms, the frequency of good results can approximate that obtained with intravenously administered agents.[10] According to Lewitan and Garcia,[6] the medium's relative safety makes it a valuable medium for peroral cholegraphy. Timesaving and economical Oragrafin Calcium Granules may be particularly useful in certain patients for whom I.V. radiography presents potential hazards, such as elderly patients and those with cardiovascular disease.

Unique among oral media, Oragrafin Calcium Granules permits same-day films of the gallbladder and the ductal system.

dosage schedule for films of gallbladder and ductal system

8 A.M.	2 packets of granules
9 A.M.	visualization of ducts
10 to 11 A.M.	visualization of gallbladder

Contraindications: Contraindicated for persons sensitive to oral iodine compounds or for patients with *combined* renal and hepatic disease or *severe* kidney impairment. Gastrointestinal disorders, which may interfere with absorption, or liver dysfunction, which may result in inadequate biliary secretion of medium, are likely to result in unsatisfactory visualization.

Precautions and Side Effects: Mild and transient nausea, vomiting, or diarrhea sometimes occur; but the incidence can be reduced by using the calcium granules and restricting the dosage to 3 Gm. Transient headache, dysuria, or abdominal pains may occur.

Hypersensitivity reactions may include urticaria, serum sickness-like reactions, and rarely anaphylactoid shock. They are more likely to occur in the individual with a history of allergy, asthma, hay fever, or urticaria and in the individual who is known to be hypersensitive to iodine compounds. Antihistamines and corticosteroids are used to control hypersensitivity reactions; but the occasional serious anaphylactoid reactions require the immediate use of epinephrine or phenylephrine, oxygen, and intravenous corticosteroids.

For full information see Package Insert.

Supply: The calcium salt (Oragrafin Calcium Granules) is available in single-dose foil packets providing 3 Gm. of calcium ipodate as Granules dispersed in flavored sucrose. The sodium salt is available in capsule form (Oragrafin Sodium Capsules) providing 0.5 Gm. sodium ipodate per capsule.

References: 1. McLuhan, M.: Understanding Media: The Extensions of Man, New York, McGraw-Hill Book Company, 1966. **2.** Sanen, F. J.: Amer. J. Roentgen. *88*:797 (Oct.) 1962. **3.** Glenn, J. C., Jr., and O'Brien, P. S.: Southern Med. J. *56*:167 (Feb.) 1963. **4.** White, W. W., and Fischer, H. W.: Amer. J. Roentgen. *87*:745 (April) 1962. **5.** Juhl, J. H., *et al.*: Radiology *80*:87 (Jan.) 1963. **6.** Lewitan, A., and Garcia, J. F.: Amer. J. Dig. Dis. *10*:219 (March) 1965. **7.** McCrory, E.: J. Tenn. Med. Ass. *58*:258 (Aug.) 1965. **8.** Root, H.: Amer. J. Roentgen. *101*: 621 (Nov.) 1967. **9.** Crummy, A. B.: Wisconsin Med. J. *65*:84 (Feb.) 1966. **10.** Saltzman, G. F.: Acta Radiol. *54*: 417, 1960. **11.** Ludin, H., and Lauchenauer, C.: Schweiz. Med. Wochenschr. *90*:471, 1960.

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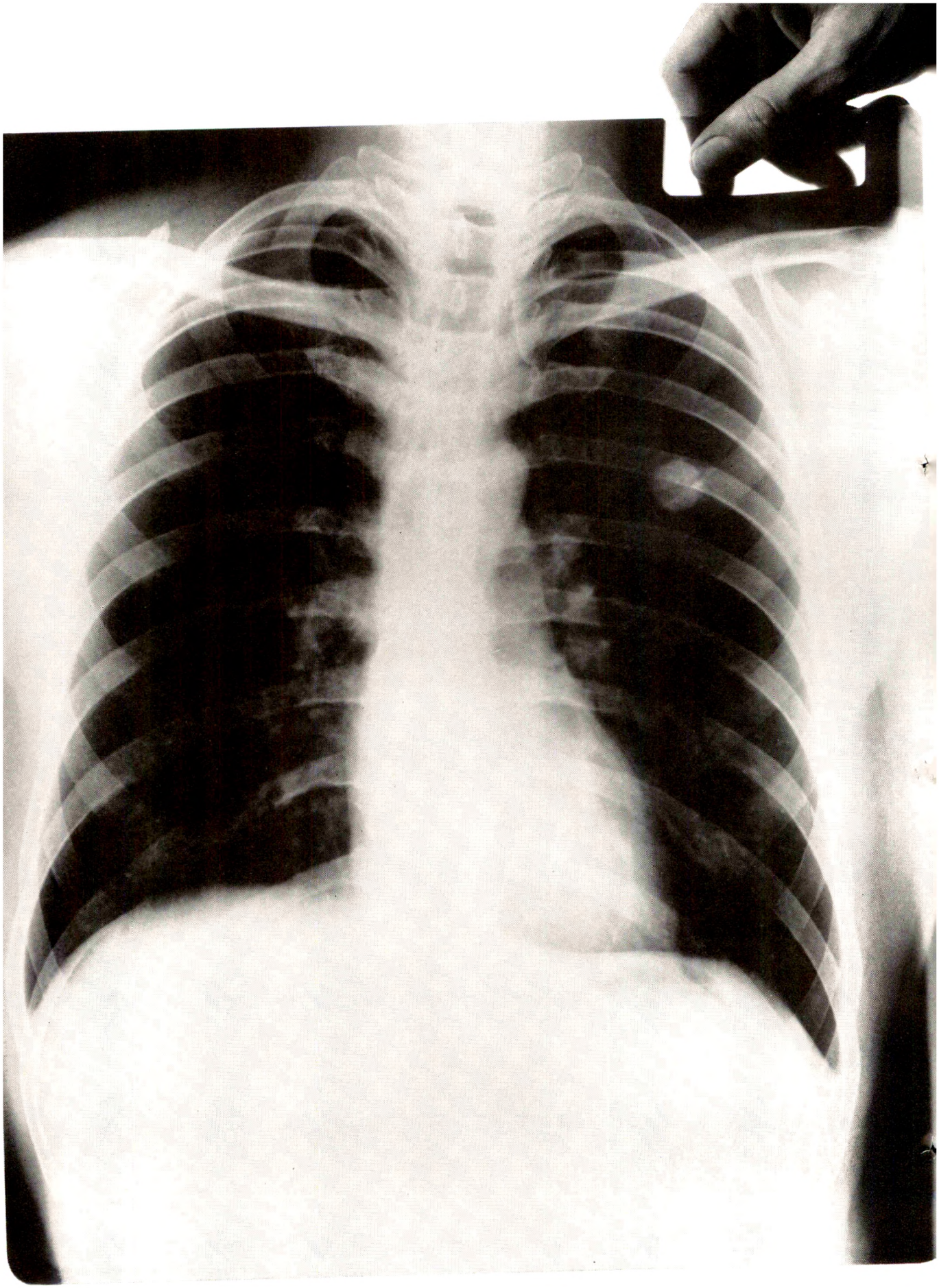
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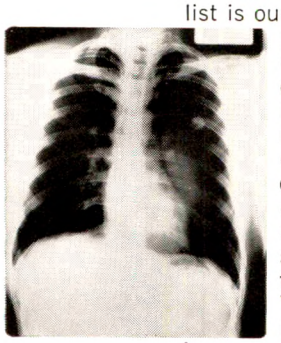


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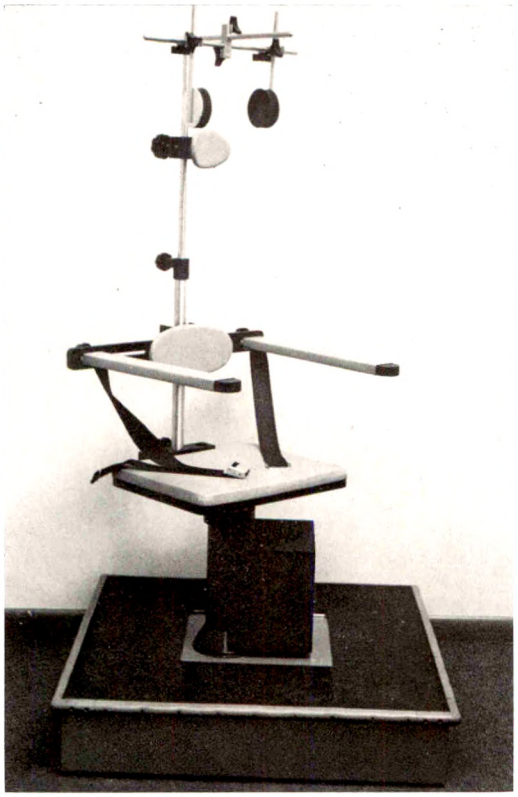


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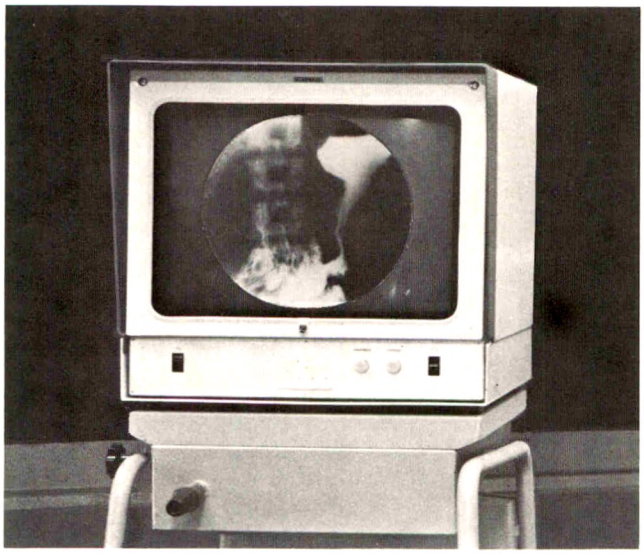
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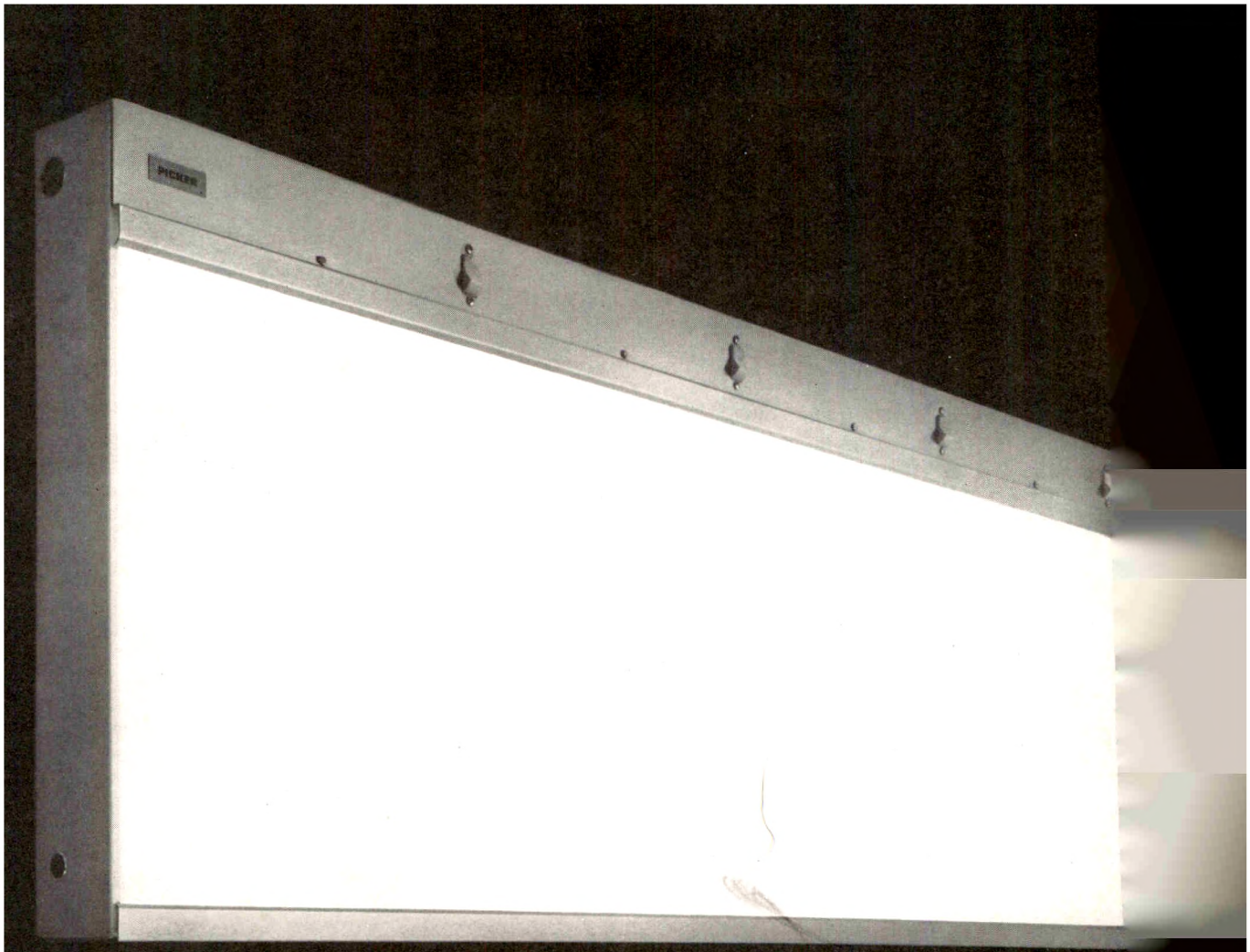
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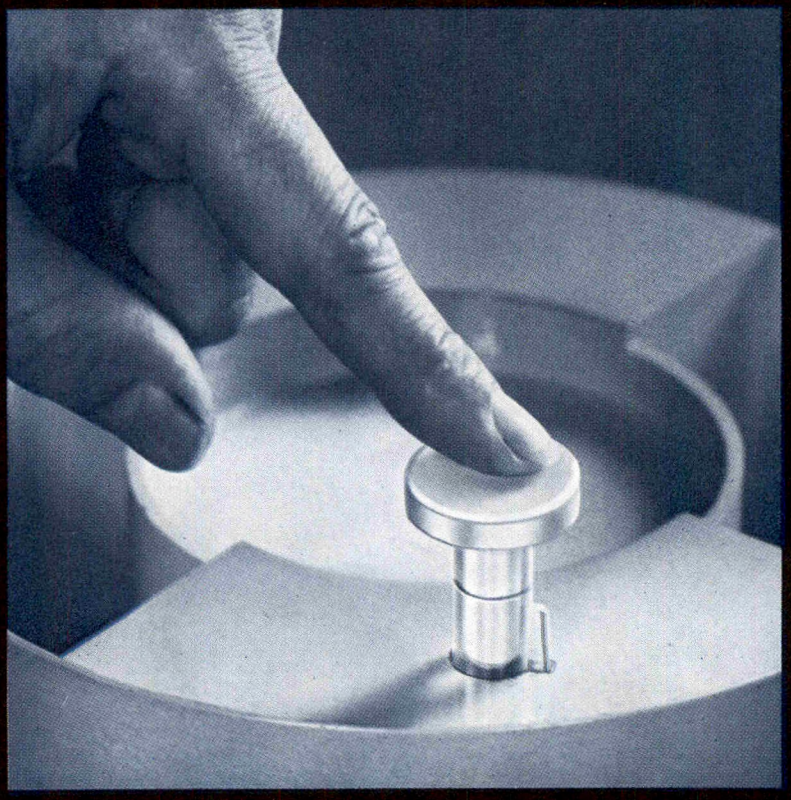
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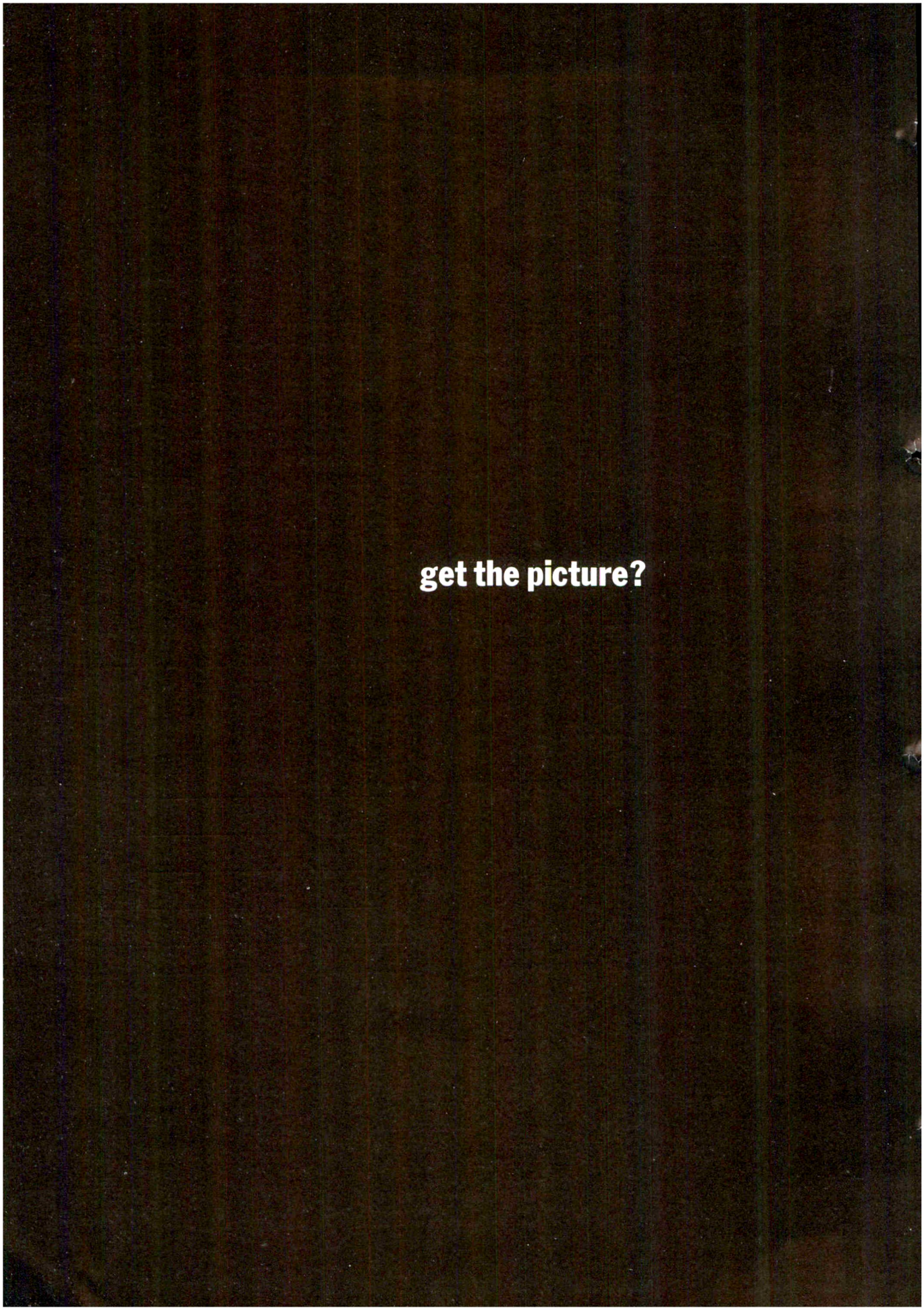
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*Causes other than disease have been occasionally reported for non-visualizing gallbladders.

Contraindications: Contraindicated in advanced hepatorenal disease or severe impairment of renal function, severe gastrointestinal disorders that prevent absorption, and in patients sensitive to iodine compounds.
Precautions: Severe, advanced liver disease may interfere with metabolism of Telepaque, thus increasing the excretory load on the kidneys. Although renal difficulty has rarely been attributed to Telepaque, renal function should be assessed before cholecystography in severe, advanced liver disease, and renal output and hepatic function should be observed for a few days after the procedure. Patients with preexisting renal disease should not receive high doses of cholecystographic media. Possible renal irritation in susceptible individuals could result in reflex vascular spasm with partial or complete renal shutdown. Caution is advised in patients with coronary disorders, especially those with recent symptoms of coronary artery disease. Blood pressure should be observed after administration of cholecystographic media to these patients. Elevation of protein-bound iodine for several months and false positive urine albumin tests (for three days) may occur after ingestion of iodine-containing cholecystographic media.

Adverse Reactions: Most reactions are mild and transitory; serious side effects are very rare. Gastrointestinal effects (diarrhea, cramps, nausea, vomiting) are the most common. Usually the diarrhea consists merely of a few loose stools, although rarely it may be severe. A mild stinging sensation during urination may occur, and rarely, skin rash, urticaria, pruritus, and flushing. One case of thrombocytopenia has been reported in a patient with a history of conjunctival hemorrhages. Subjective complaints have been: dryness of throat, burning on swallowing, heartburn, sore throat, dizziness, and headache.

Usual Dosage: 3 Gm. (6 tablets) at night after a light supper.

Supplied: Tablets of 500 mg., envelopes of 6 tablets, boxes of 5 and 25 envelopes; also bottles of 500.

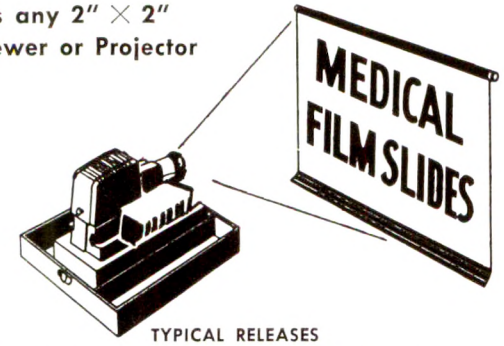
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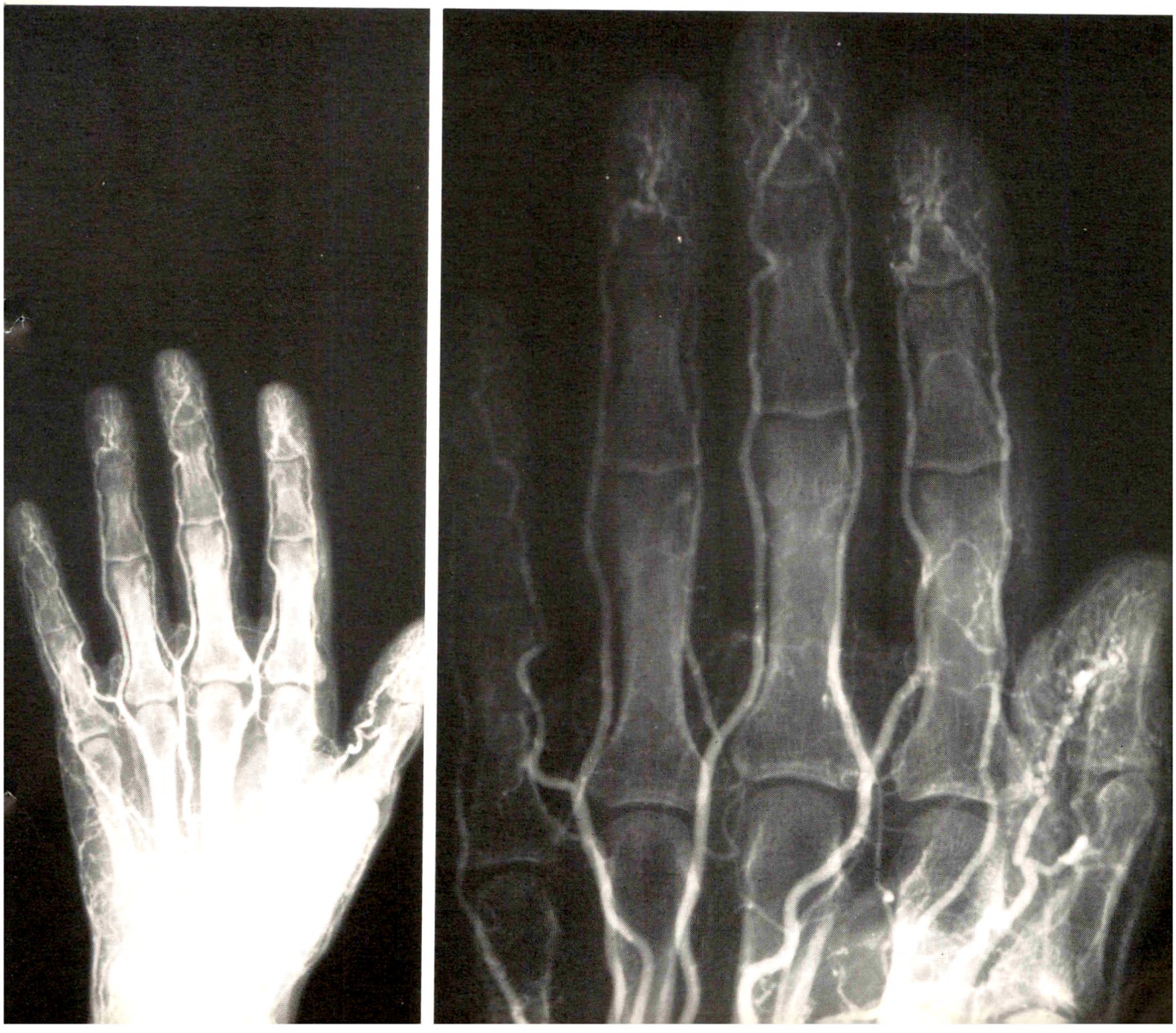
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a research concept in contrast visualization

for better definition of disease: documenting differences between contrast agents

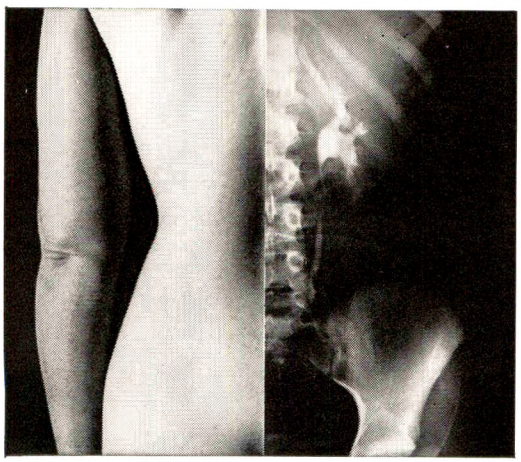
No. 1 in a series:

Renografin-60 (meglumine diatrizoate injection) preferred in a study of pyelographies of 2,234 patients.

In a new large scale study,[1] "...to determine which medium would produce adequate visualization of the urinary tract with the fewest toxic effects on the patient," Macht *et al.* have compared Renografin-60 with 2 other contrast agents.

Data were analyzed in 2,234 unselected (consecutive) patients, according to age, sex, and general disease group for the study population as a whole. The first 683 patients received 50% diatrizoate sodium solution, the next 921 patients received Renografin-60, and the final 630 patients received 66.8% sodium iothalamate solution.[1]

criteria for quality and comparative safety The contrast agents were evaluated for quality of diagnostic films as follows: films showing a dense concentration of contrast medium with filling and visualization of all major and minor calyces, infundibula, pelves and almost all of each ureter were listed as "good"; films showing less concentration with incomplete visualization of all portions of urinary tract but sufficient to produce diagnostically adequate films were listed as "fair"; films showing unsatisfactory visualization of urinary tract, or films which could not be interpreted, as "poor." The media were also evaluated as to incidence of the following side effects: nausea, vomiting, fainting, shock or severe reaction, hiccups, hives, pain in arm, sneezing, hot flushes, stuffiness of nose or ears.[1]



The following chart* shows comparative results of the 3 media according to age category:

quality of pyelograms and side effects expected in standard population of 1,000 patients by age, according to type of medium used

medium used and type of patient	standard population	quality of pyelograms good	fair	poor	with side effects
meglumine diatrizoate					
all ages,	1,000	827	123	50	41
0-19†	126	122	3	1	3
20-49	415	374	35	6	27
50-69	315	240	51	24	9
70 or older	144	91	34	19	2
diatrizoate sodium					
all ages,	1,000	782	134	84	72
0-19	126	115	6	5	7
20-49	415	378	26	11	40
50-69	315	227	64	24	19
70 or older	144	62	38	44	6
sodium iothalamate					
all ages,	1,000	883	81	36	54
0-19	126	122	4	0	7
20-49	415	393	20	2	29
50-69	315	269	32	14	13
70 or older	144	99	25	20	5

*Adapted from Macht[1] †In some patients in this age group, higher than recommended doses were used.

In theory: "The choice of contrast agent should ideally be individualized according to the age, sex, and disease group of the patient in order to obtain a high probability of complete visualization of the urinary tract with low probability of adverse side effects."[1]

In practice: "The choice is to be made...on the basis of the agent which gives the best concentration and the fewest side effects in the greatest number of patients regardless of age, sex, or disease category."[1]

In order of preference: Although Renografin-60 was not rated highest in all categories, the authors feel that their preference of the contrast media for intravenous pyelography would be: first, Renografin-60; second, sodium iothalamate; third, diatrizoate sodium.[1]

For brief summary of prescribing information, please refer to the end of this advertisement.

definition of safety...

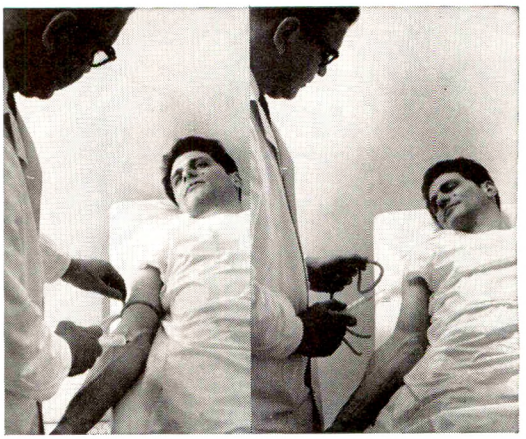
demonstrated in animals... Since meglumine diatrizoate is also used for cerebral angiography, toxicity studies of administration via the carotid artery are therefore of interest. Fischer and Eckstein[2] designed angiographic studies in animals in which procedures were very similar to clinical angiography, and which yielded data that was quantitative, graphic and nonsubjective.[2] According to the authors: "We selected the alterations in arterial blood pressure, venous pressure, heart rate and rhythm, the electrocardiogram and end-expiratory CO_2 concentration resulting from experimental cerebral angiography as refined, sensitive indications of the toxicity of a particular contrast material."[2] Their results of measured cardiovascular functions in dogs indicated that meglumine diatrizoate was far less toxic than four other contrast media.[2] As Fischer and Cornell reported in a later study: "Despite the testing of more highly concentrated solutions and larger doses, the cardiovascular responses [in dogs] from methylglucamine [meglumine] salts were much less than from sodium salts, an observation consistent with previous experiments."[3]

Other investigators have documented the comparative safety of meglumine salts in experimental studies. In order to determine reaction and tolerance of the intestines, Cooley[4] injected meglumine diatrizoate into mesenteric arteries of dogs and found no damage. Gensini *et al.*[5] reported that cardiovascular responses with it were almost identical to blood transfusions.

theory of lower toxicity with meglumine... Gensini and DiGiorgi have offered a hypothesis to explain their findings of lesser toxicity with experimental intravascular injections of methylglucamine (meglumine) salts. "When a relatively undiluted amount of sodium salts of a contrast agent is injected in an artery and carried by the blood stream toward the capillary bed, its molecules rapidly dissociate and readily diffuse through the capillary membrane and into the tissue. There, both the toxic effect of the iodine-containing organic radical and the increased concentration of sodium will readily manifest themselves. At equal concentrations of sodium, the end results will closely reflect the intrinsic toxicity of the iodine-containing organic radical on the tissues...."[5]

"In the case of the methylglucamine compounds, the same dissociation takes place. However the larger methylglucamine molecule, rich in hydrogen bonds, apparently either limits the migration of the organic radicals outside the vessel or at least minimizes their effects on the cellular metabolism."[5]

proved in practice... Paralleling similar findings in animals, clinicians have reported a generally lower



incidence of untoward reactions with Renografin-60 in urologic and cerebrovascular use. However, as with all intravascularly injected contrast agents, the possibility of severe reactions should be kept in mind (see Contraindications, Precautions and Side Effects below). In one study of over 600 urologic patients, the investigators reported that Renografin-60 produced urograms of diagnostic quality with a 6% incidence of side effects. The authors concluded: "It is hard to believe that any drug introduced intravenously could be so well borne by so many patients...."[6]

In a 74-patient study,[7] comparing Renografin-60 with diatrizoate sodium in carotid arteriography, Shealy commented: "With confused patients who are to have arteriography under local anesthesia, it is particularly desirable to have an agent that causes little pain." In this study, since "...60 per cent Renografin has resulted in considerably less pain than 50 per cent or 45 per cent [diatrizoate sodium]...we have converted to the routine use of 60 per cent Renografin for carotid arteriography; an additional 1,500 arteriograms done with 60 per cent Renografin have been quite satisfactory."[7]

better tolerated even in pediatrics... Citing some difficulties in administering contrast agents intravenously to children, Strasser *et al.*[8] selected Renografin-60 for intramuscular use in excretion urography in 16 pediatric patients because of the mild and relatively few reactions consistently associated with its use. The authors concluded: "The almost complete absence of any kind of local effect from its injection into the gluteal muscle and the absence of any serious reactions, local or systemic, indicate the safety of the medium."[8]

For brief summary of prescribing information please refer to the end of this advertisement.

definition of efficacy...

a thoroughly investigated meglumine salt Extensively evaluated for over a decade, Renografin has been consistently shown to yield a high percentage of diagnostic quality films in many phases of contrast visualization.

Upon intravenous injection, Renografin is rapidly carried to the kidneys and is so well concentrated that renal passages—including renal pelvis, ureters and bladder—may be clearly visualized. This medium also provides high contrast vasography in visualization of the cerebral vessels and the peripheral arteries and veins.

proved diagnostic excellence... In a comparative study[9] of 3 contrast agents used in cerebral angiography by Doehner (comprising a cross section of an average neurosurgical practice), Renografin-60 was equal in the arterial phase and slightly superior in the venous phase of the examination.

Findings of a previously cited study by Orr *et al.*,[6] in intravenous pyelography, also attest to the diagnostic excellence of Renografin-60. "Satisfactory roentgenograms of the kidneys were obtained in 636 (97%) of the cases, demonstrating the great diagnostic value of this procedure." And, as noted previously, Shealy found the contrast agent to be "quite satisfactory" in 1,500 carotid arteriograms.[7]

References: 1. Macht, S. H.; Williams, R. H., and Lawrence, P. S.: Amer. J. Roentgen. 98:79 (Sept.) 1966. **2.** Fischer, H. W., and Eckstein, J. W.: Amer. J. Roentgen. *86*:166 (July) 1961. **3.** Fischer, H. W., and Cornell, S. H.: Radiology *85*:1013 (Dec.) 1965. **4.** Cooley, R. N., *et al.*: Angiology *15*:107 (Mar.) 1964. **5.** Gensini, G. G., and DiGiorgi, S.: Radiology *82*:24 (Jan.) 1964. **6.** Orr, L. M.; Campbell, J. L., and Thomley, M. W.: J.A.M.A. *169*:1156 (Mar.) 1959. **7.** Shealy, C. N.: J. Neurosurg. *20*:137 (Feb.) 1963. **8.** Strasser, N. F., *et al.*: Radiology *79*:408 (Sept.) 1962. **9.** Doehner, G. A., and Brugger, G. E.: New York J. Med. *60*:4022 (Dec.) 1960.

Contraindication

A history of sensitivity to iodine per se or to other contrast media is not an absolute contraindication to the use of meglumine diatrizoate.

Precautions and Side Effects

Severe, life-threatening reactions are rare; when they occur they suggest hypersensitivity. A personal or family history of asthma or allergy warrants special attention and may predict, more accurately than pretesting, the likelihood of a reaction, although not the type nor severity of the reaction in the individual.

The value of any pretest is questionable. The pretest most performed is the slow injection of 0.5-1.0 cc. of the preparation into a peripheral vein. An impending reaction is often indicated by transient burning and flushing, pain, "jump-like" reactions, respiratory difficulty, faintness, sneezing, itching, nausea, vomiting or urticaria. Should the test dose produce an untoward response, the necessity for continuing the examination should be re-evaluated. Antiallergic drugs may be used to advantage. In a few cases, the reactions to the test dose have been extremely severe.

The more serious anaphylactoid reaction requires immediate treatment and may occur despite a negative sensitivity test. An emergency tray consisting of vasopressor drugs, epinephrine hydrochloride 1:1000, methoxamine (Vasoxyl) or metaraminol bitartrate (Aramine), and glucose and saline is recommended. Oxygen and instruments to guarantee a clear airway must be readily available.

Caution must be exercised, especially in cerebral angiography in extreme age, in severely debilitated patients and in those with marked or severe hypertension, advanced arteriosclerosis, cardiac decompensation, recent cerebral embolism, or thrombosis, chronic pulmonary emphysema and in cyanotic infants.

For full details the Package Insert should be read.

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Available in 30 cc. vials or 25 cc. ampuls.

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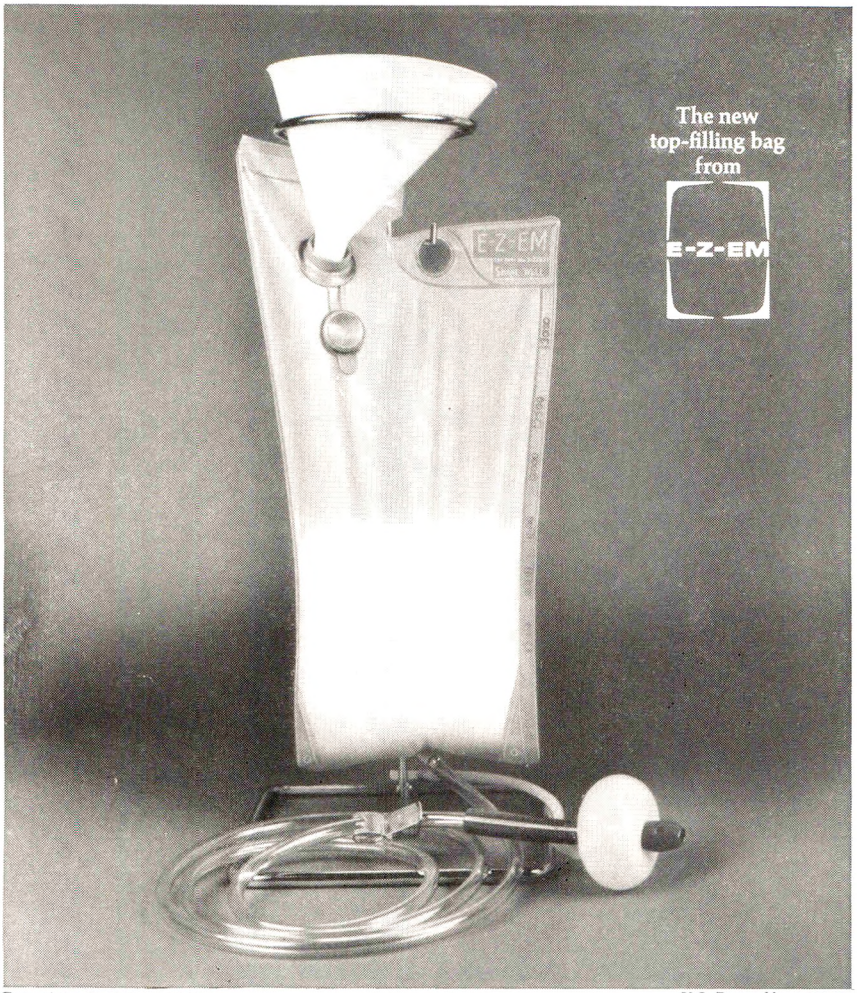
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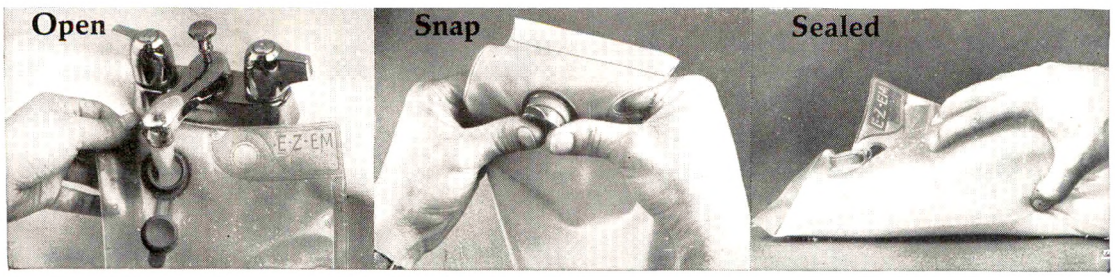
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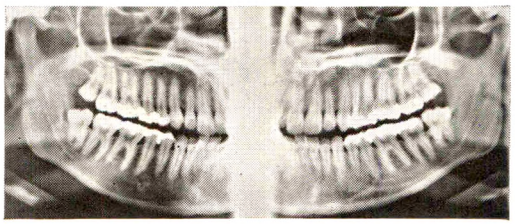


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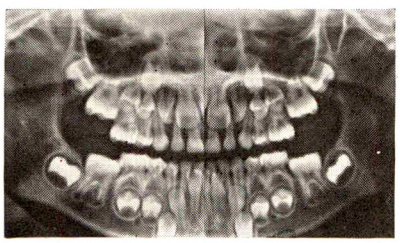
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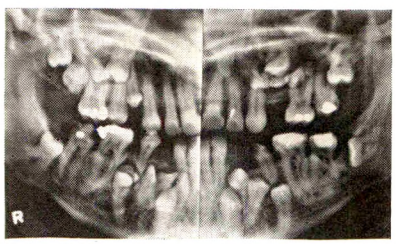
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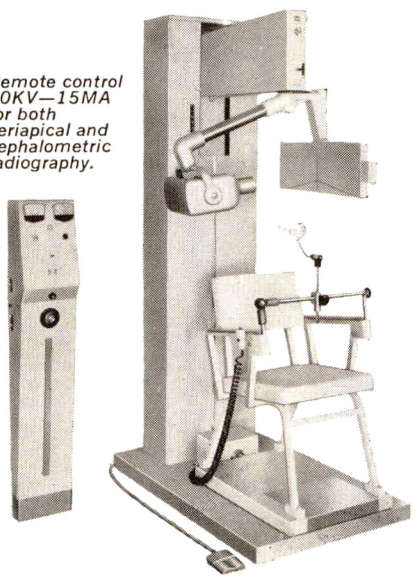


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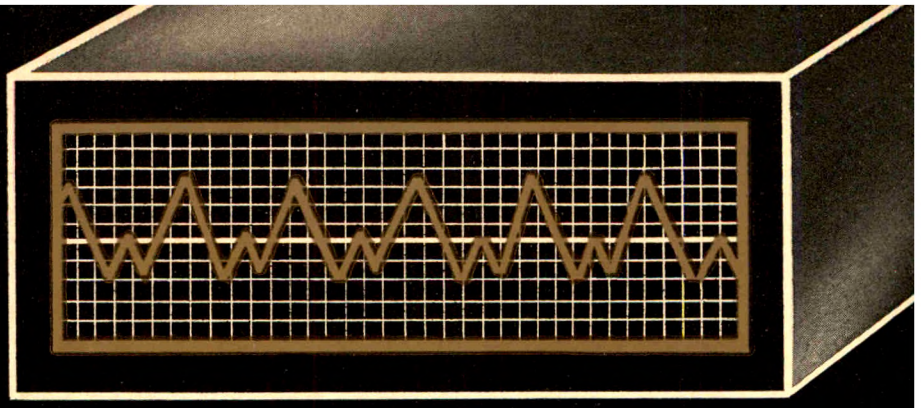
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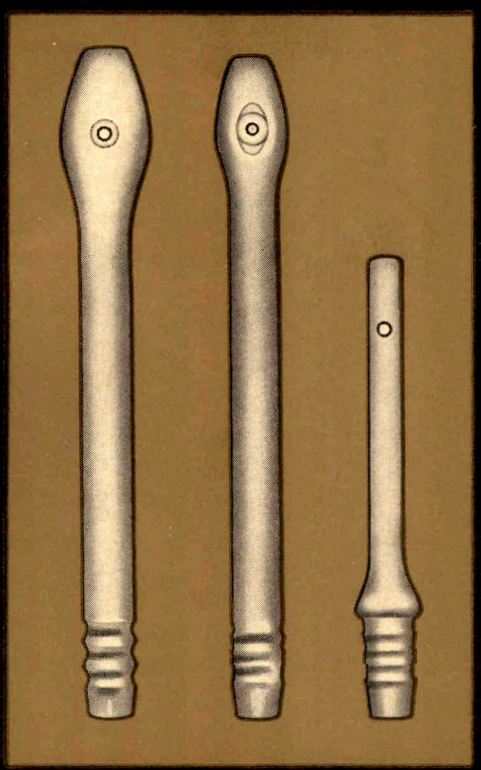


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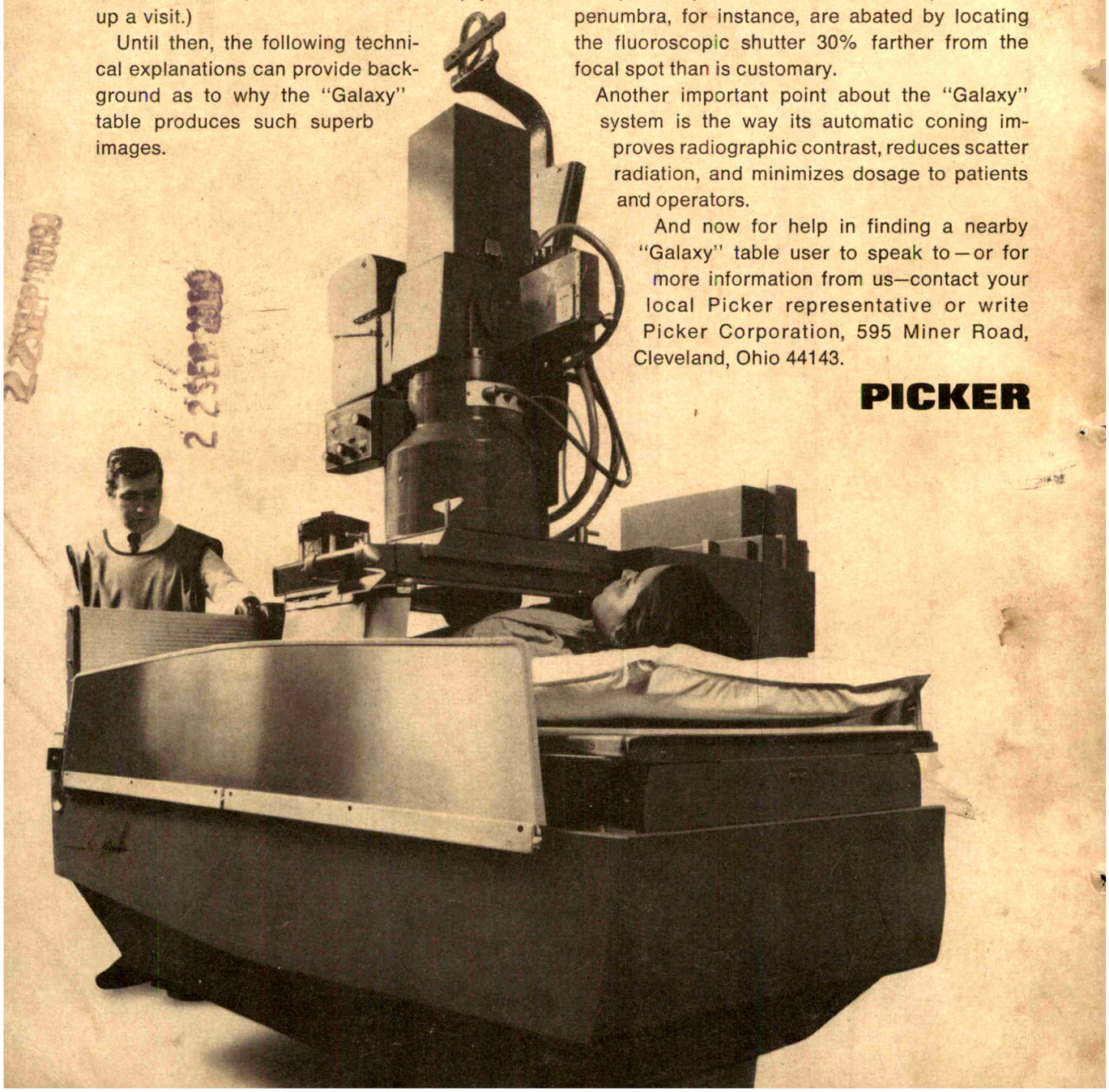
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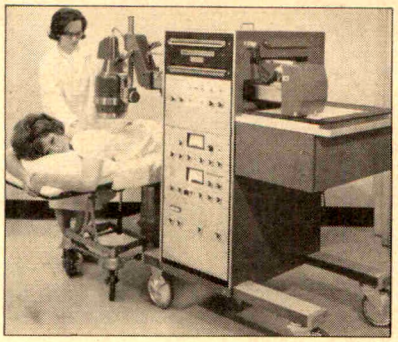
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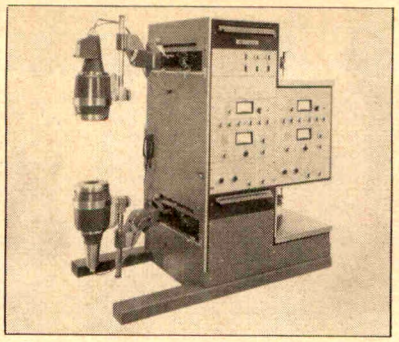
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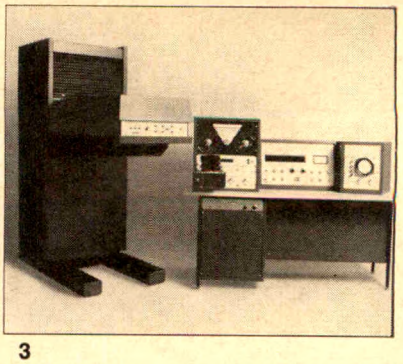
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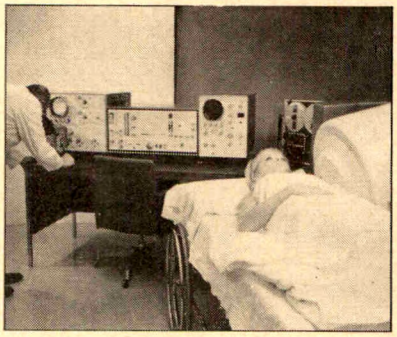
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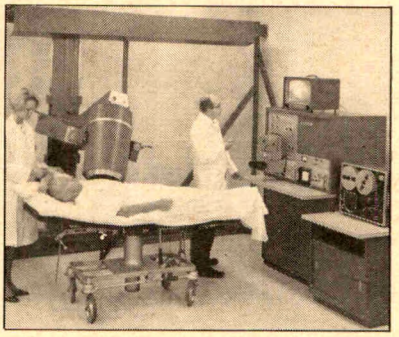
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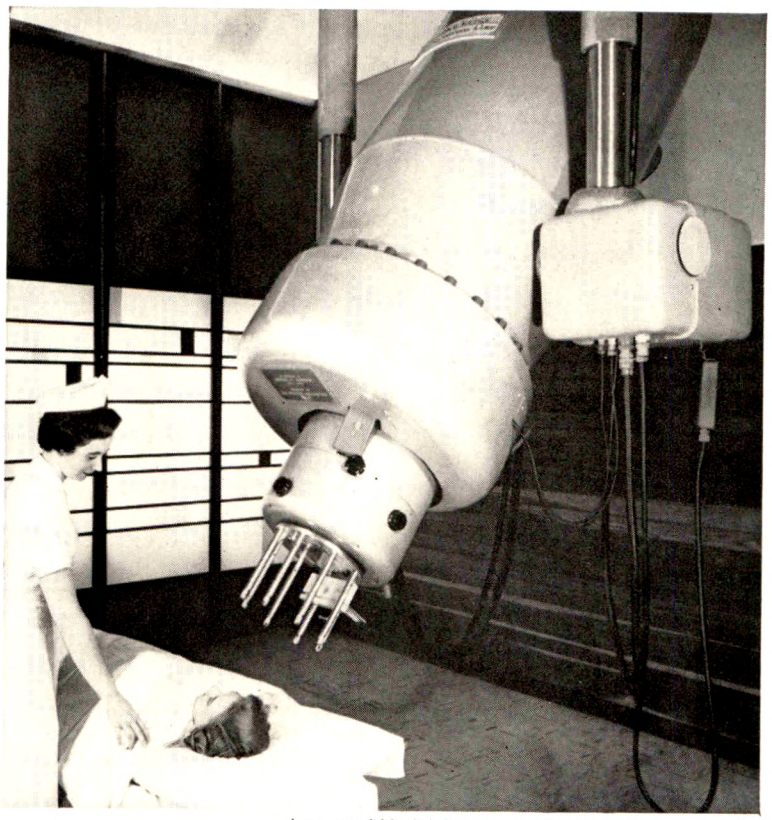
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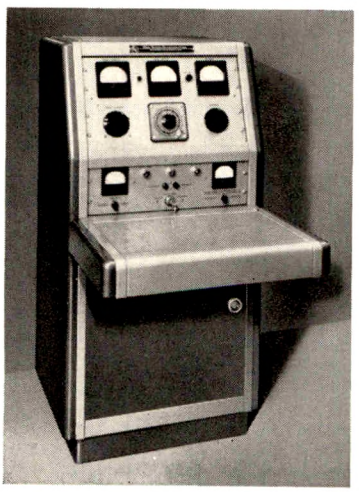


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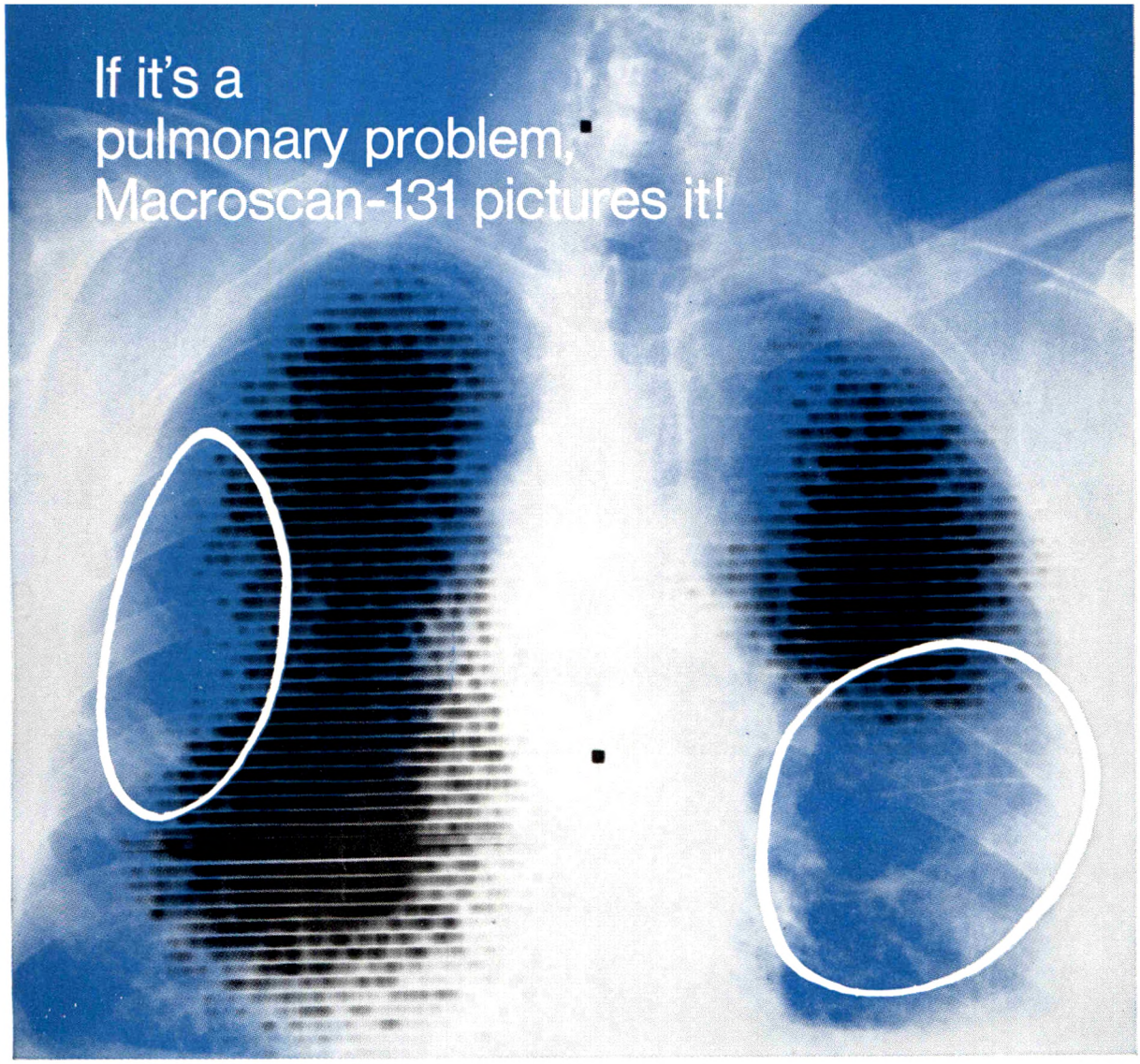
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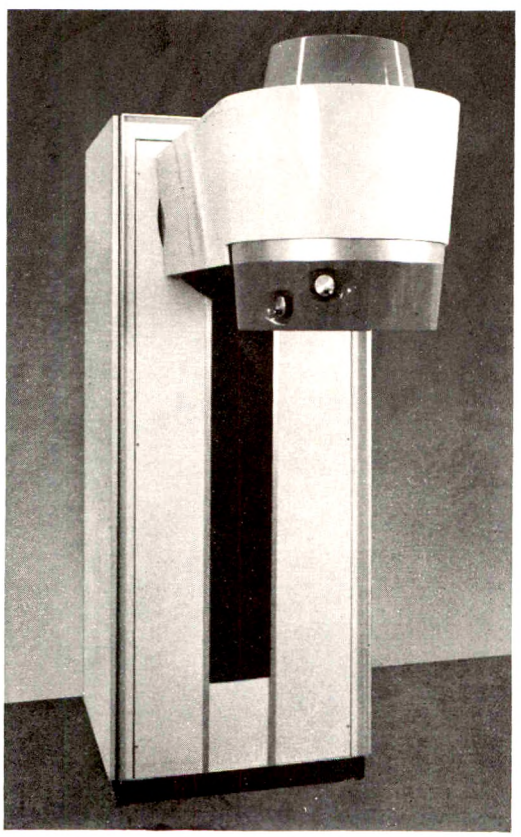
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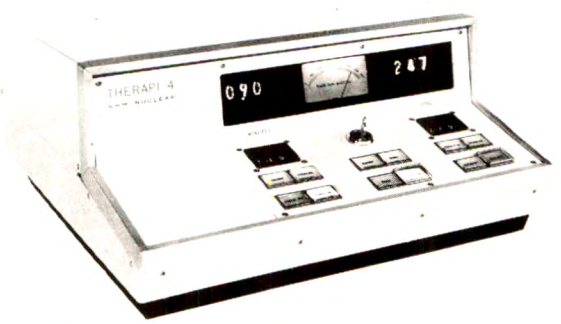
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The Therapi 4—medical linear accelerator



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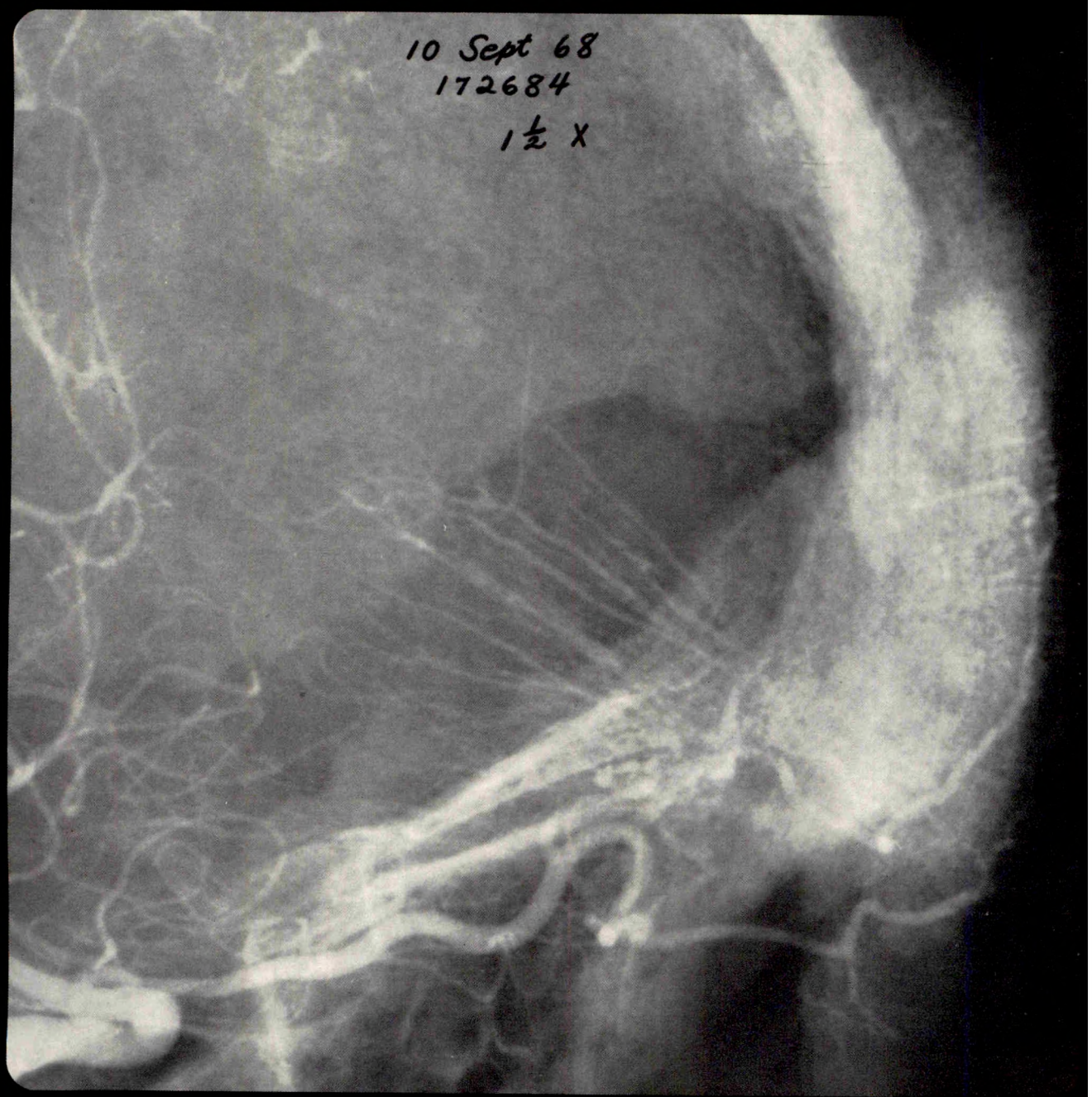
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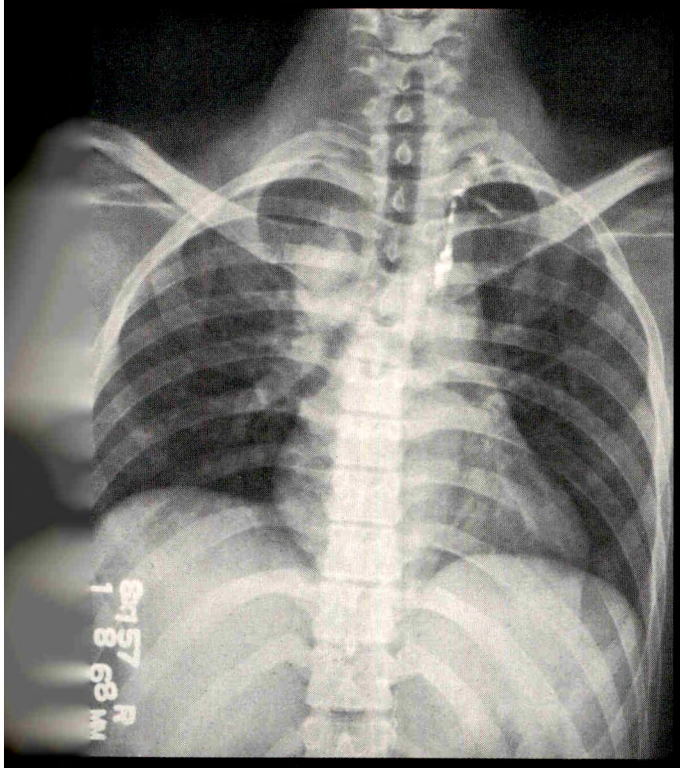


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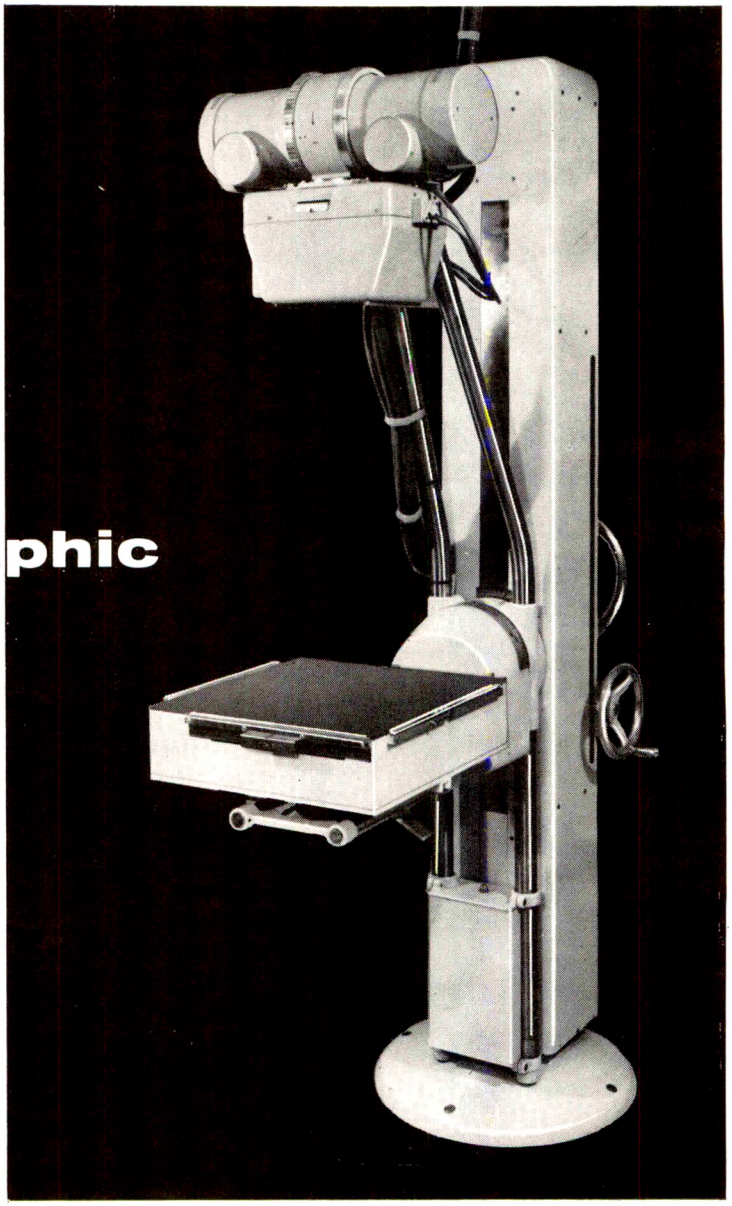
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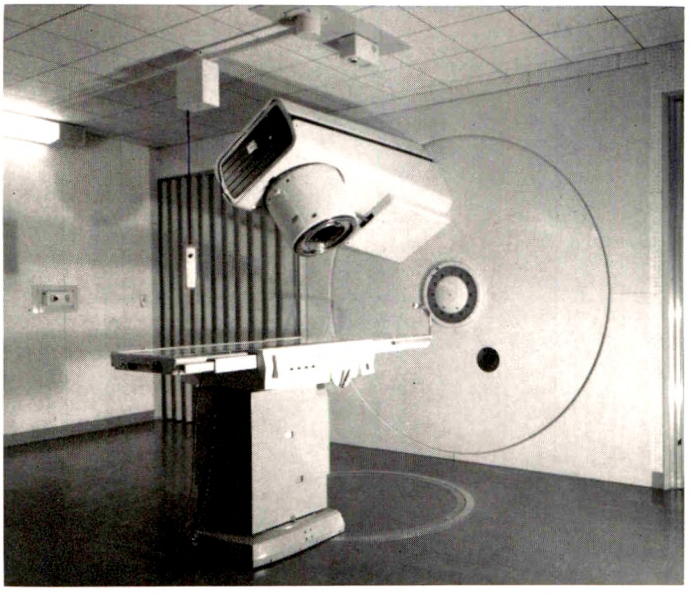
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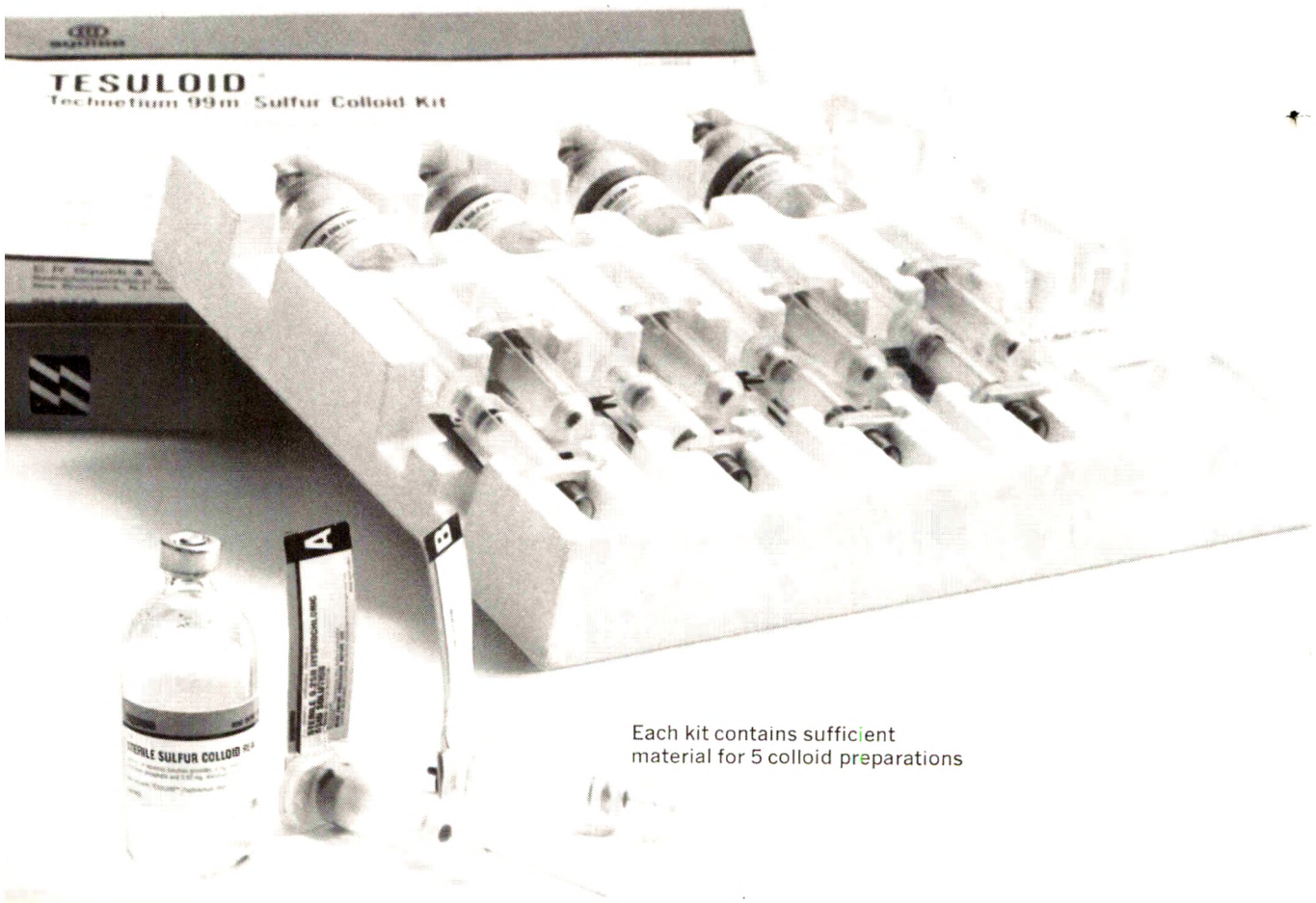


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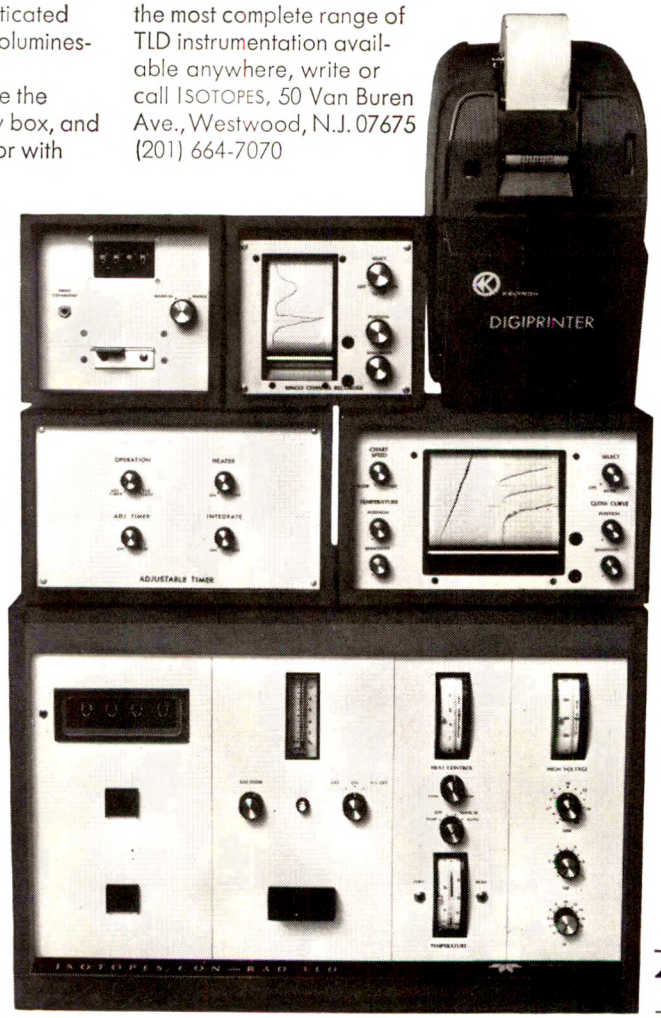
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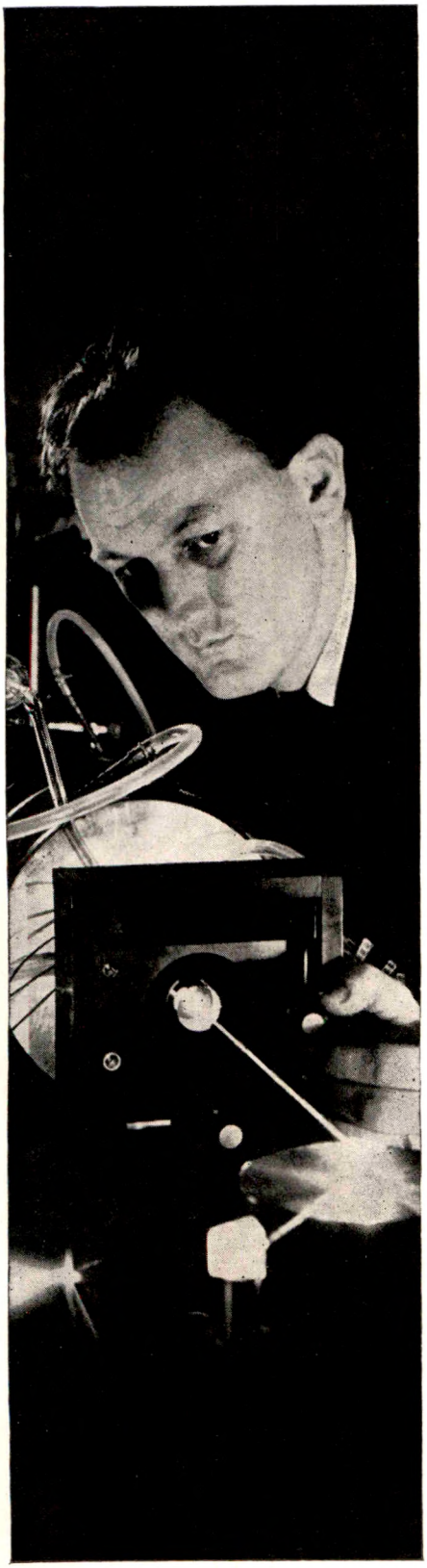
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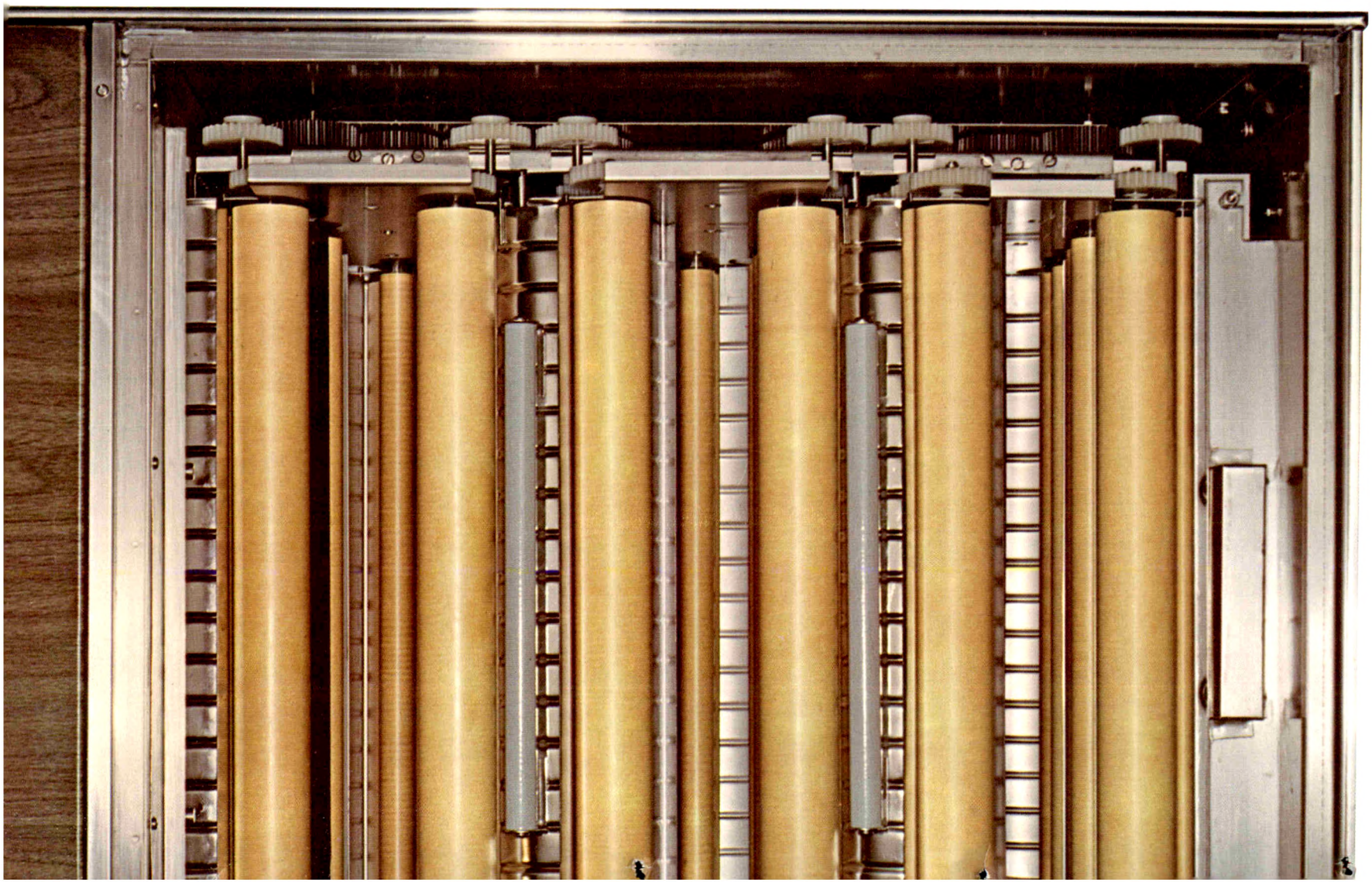
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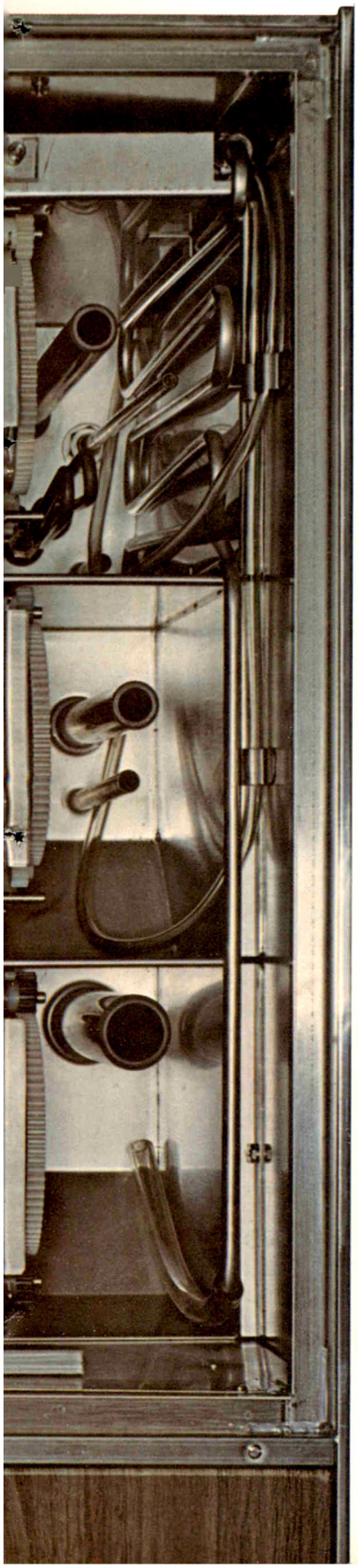
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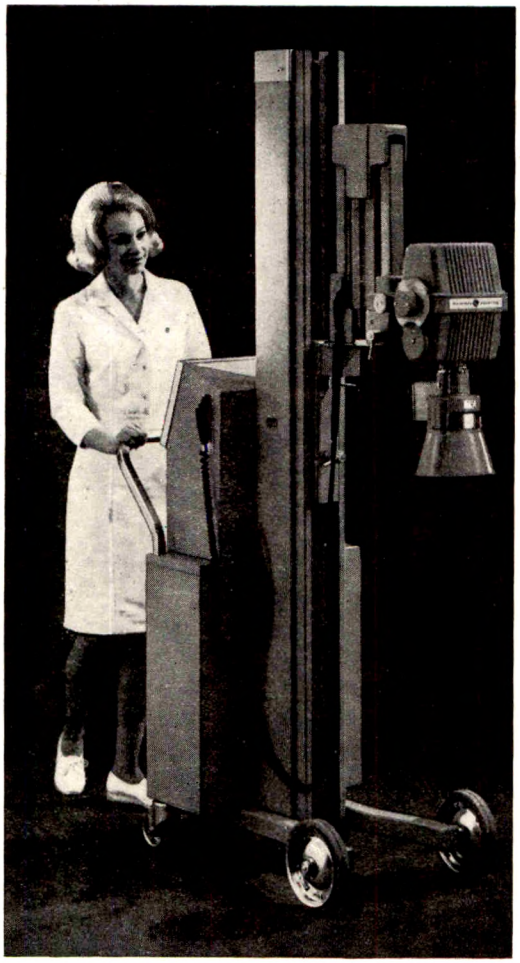
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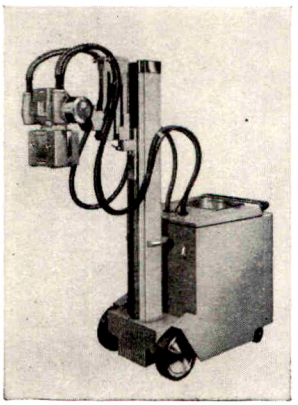
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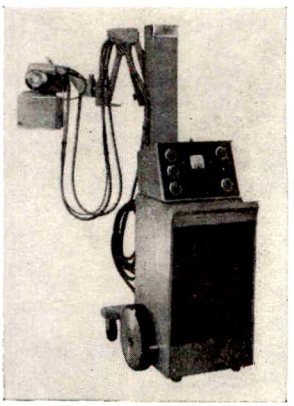
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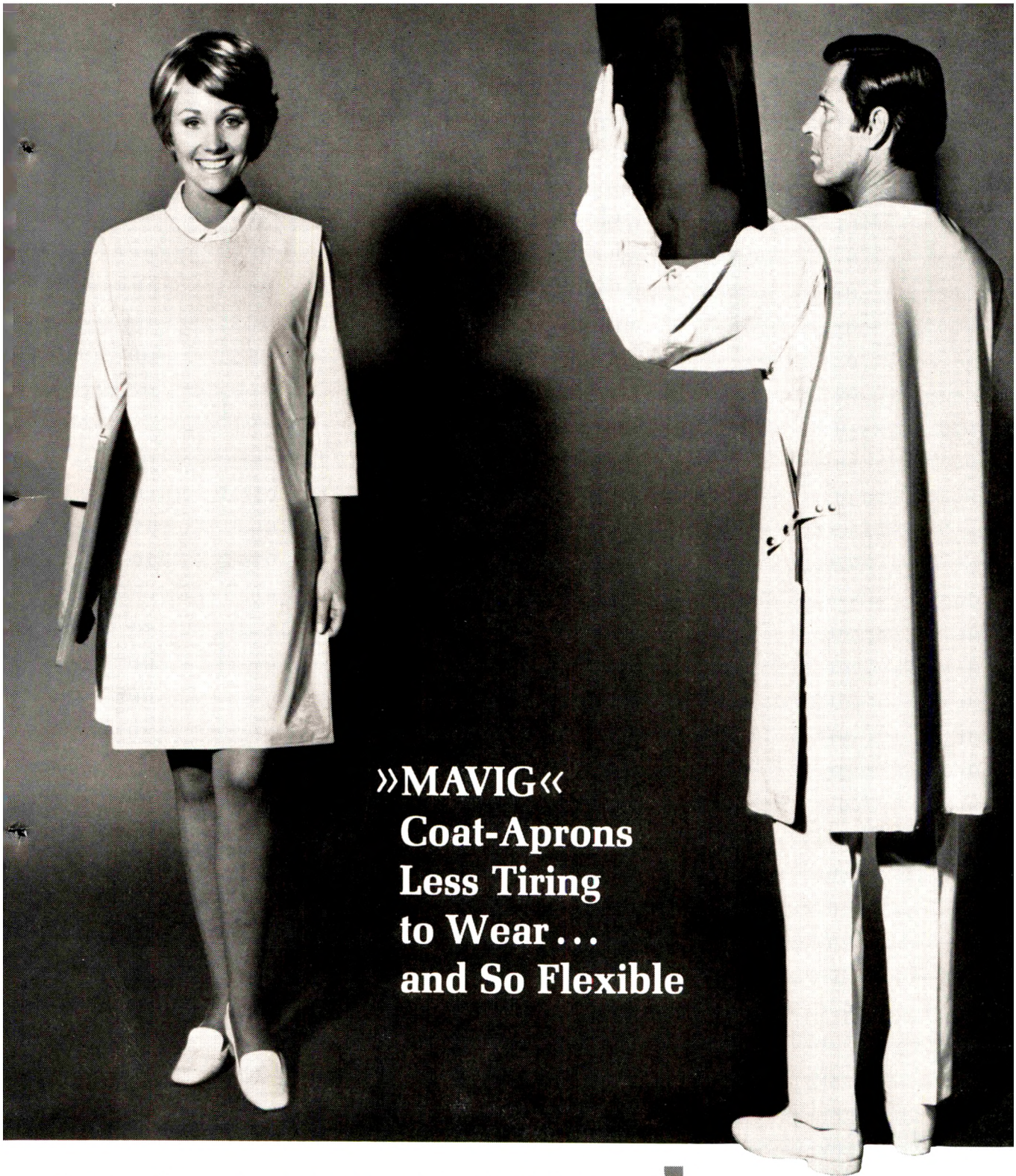
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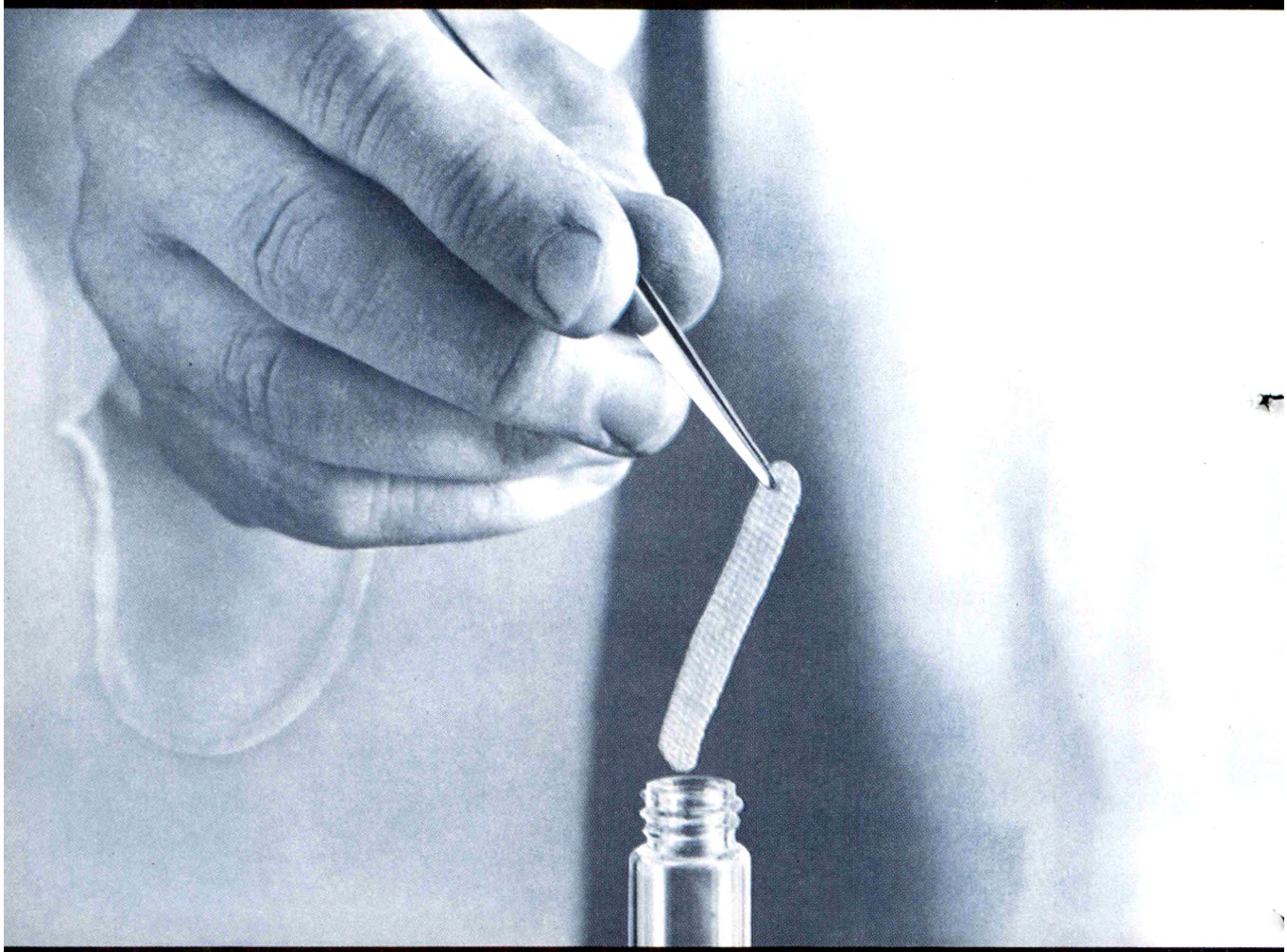
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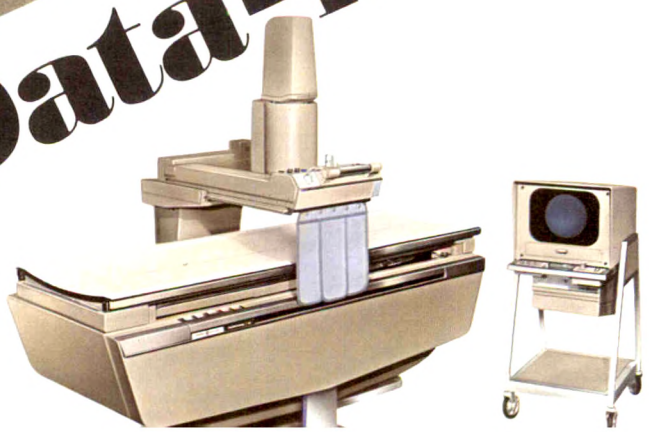
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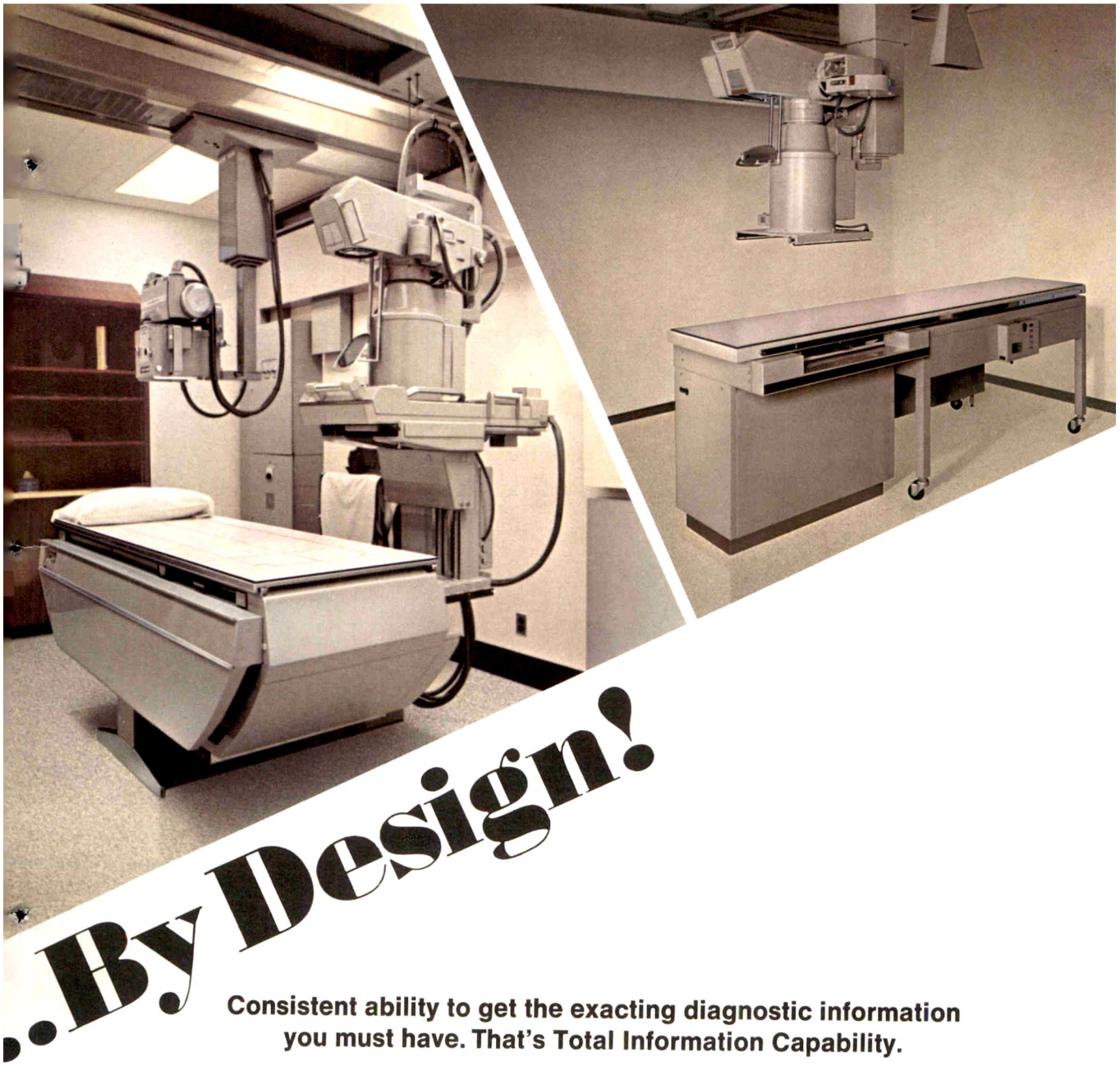
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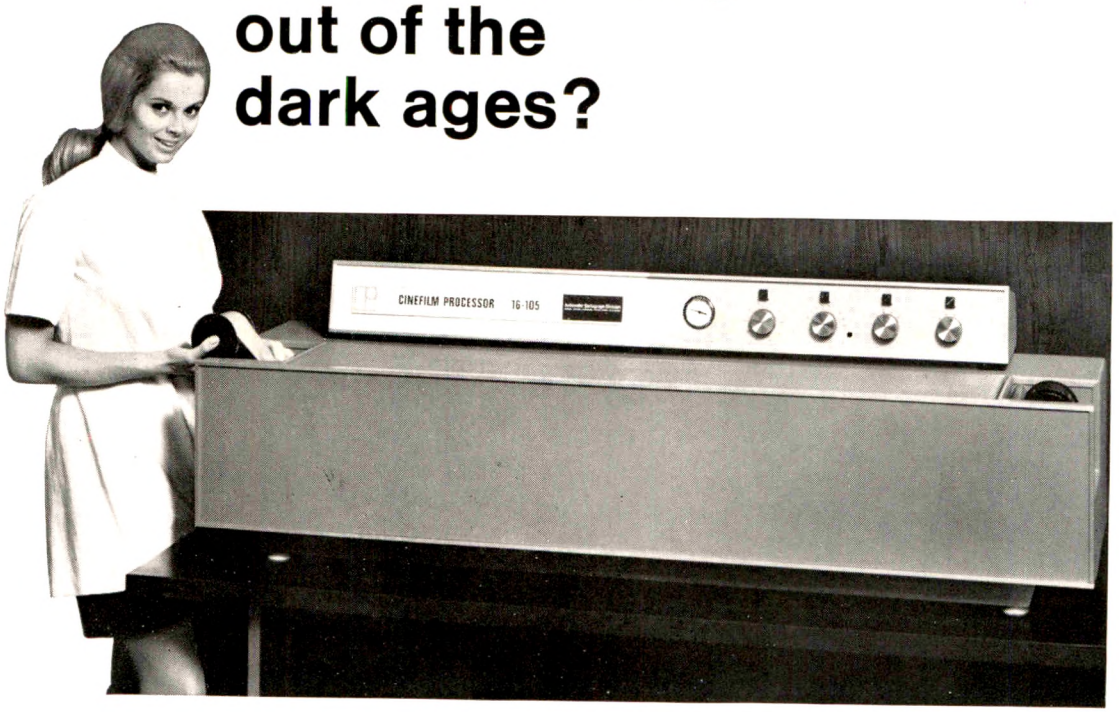


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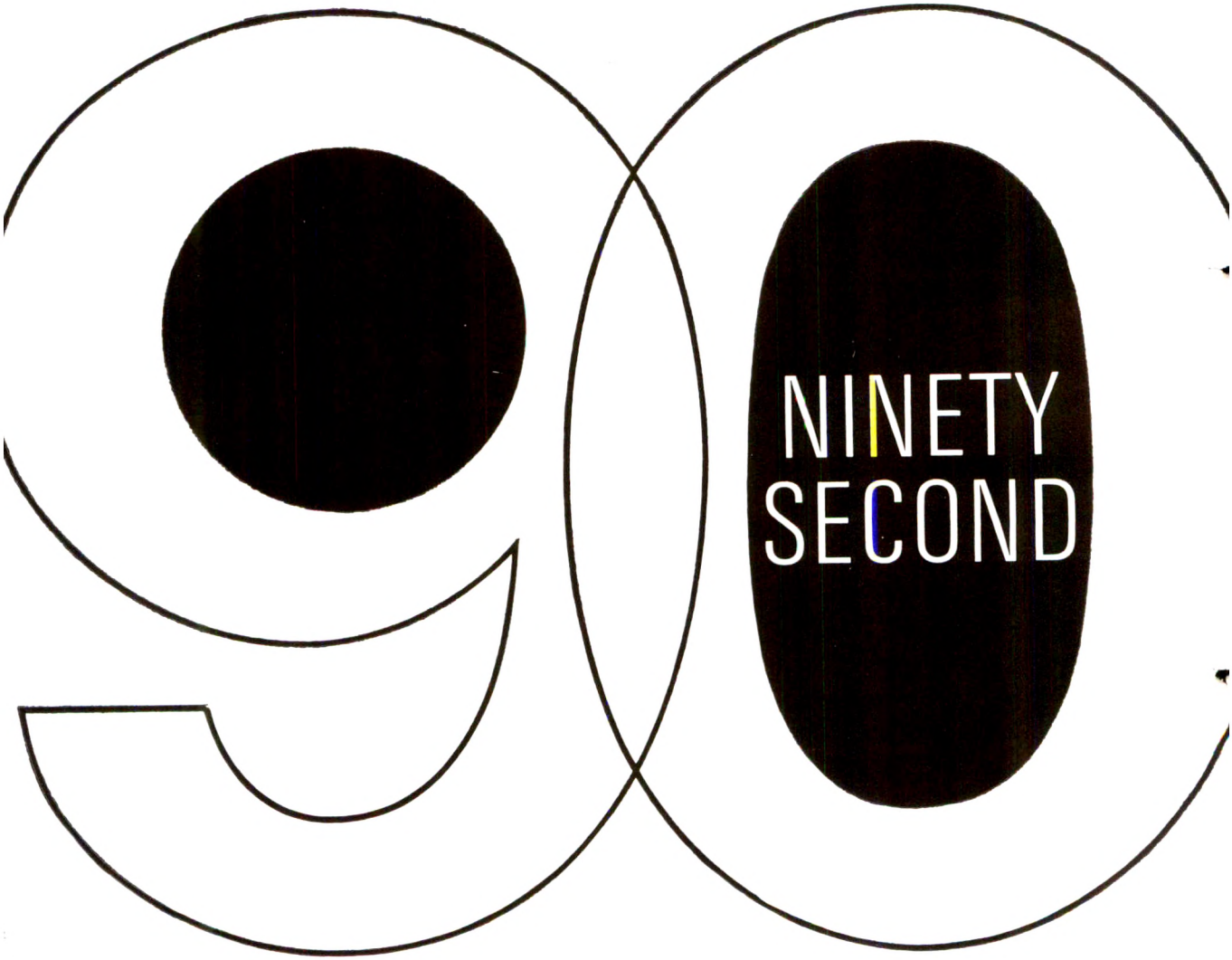
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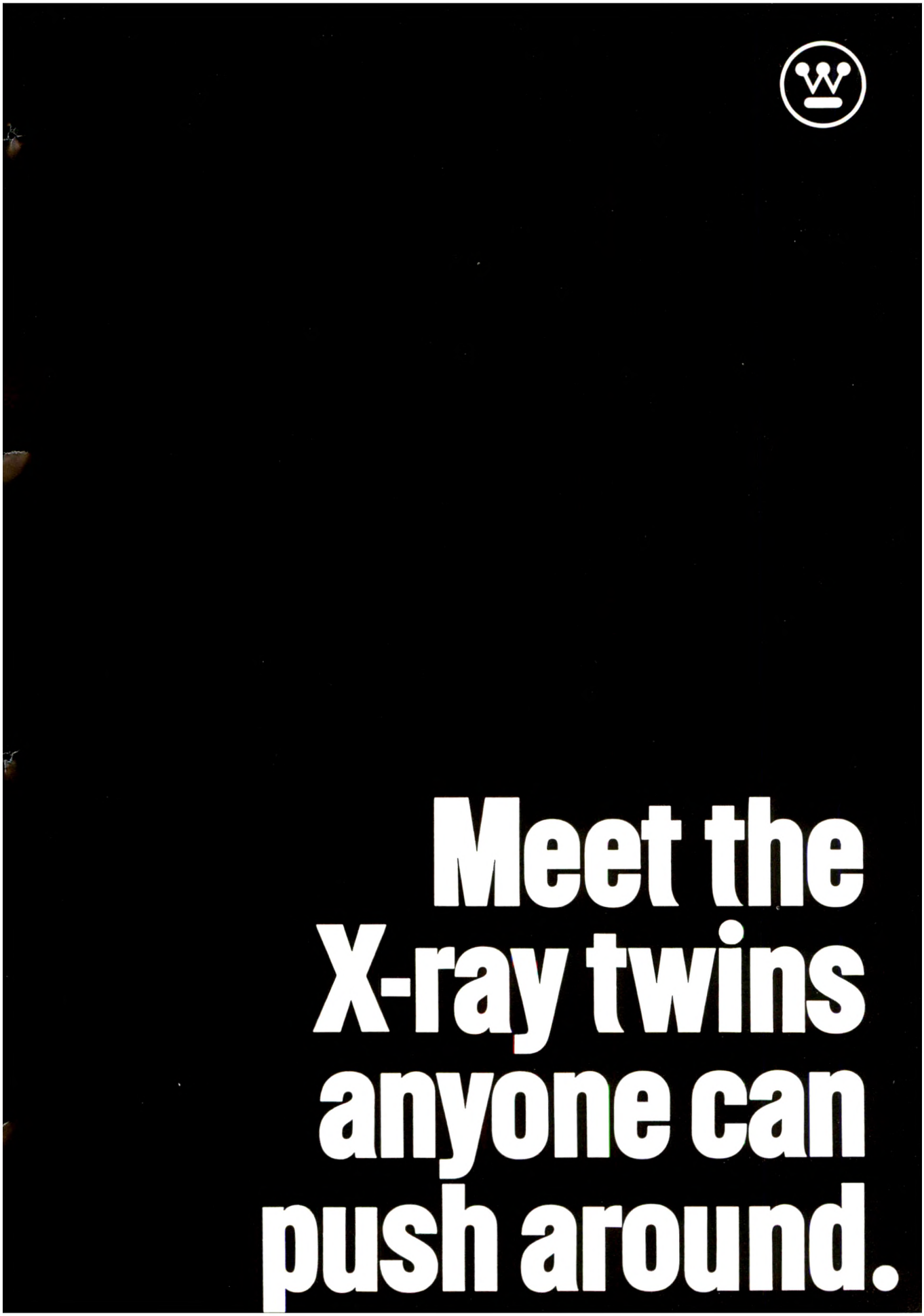
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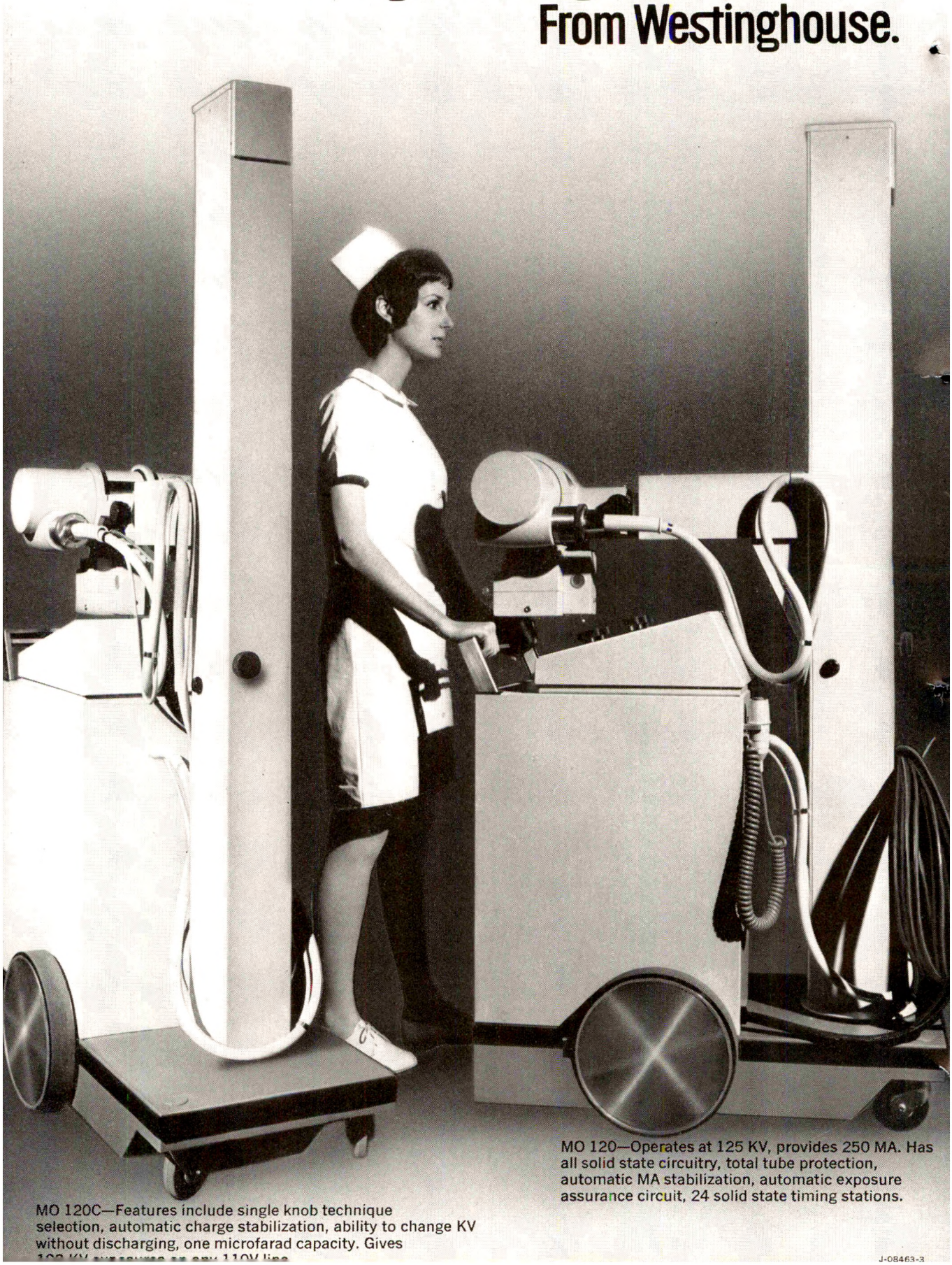
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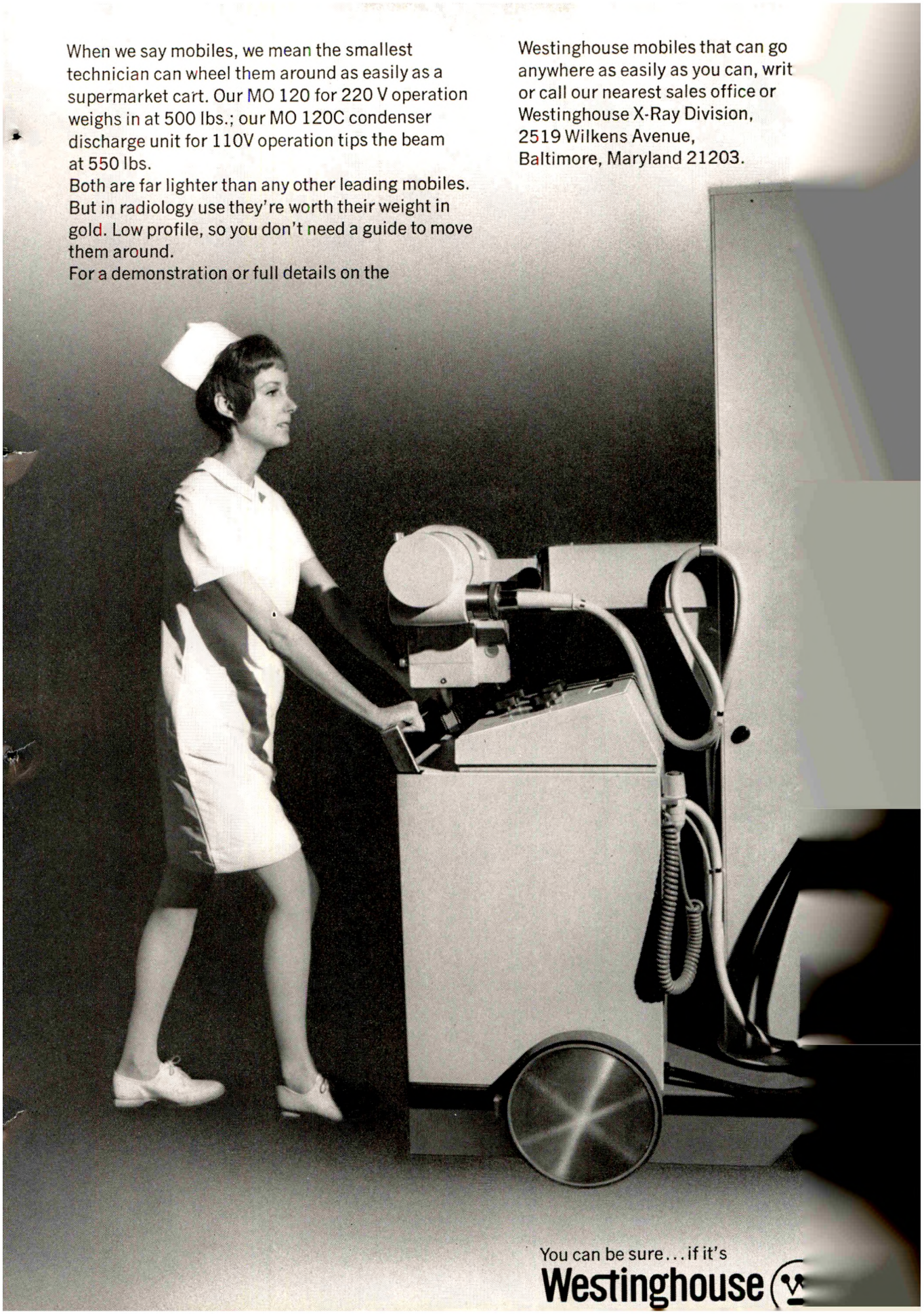
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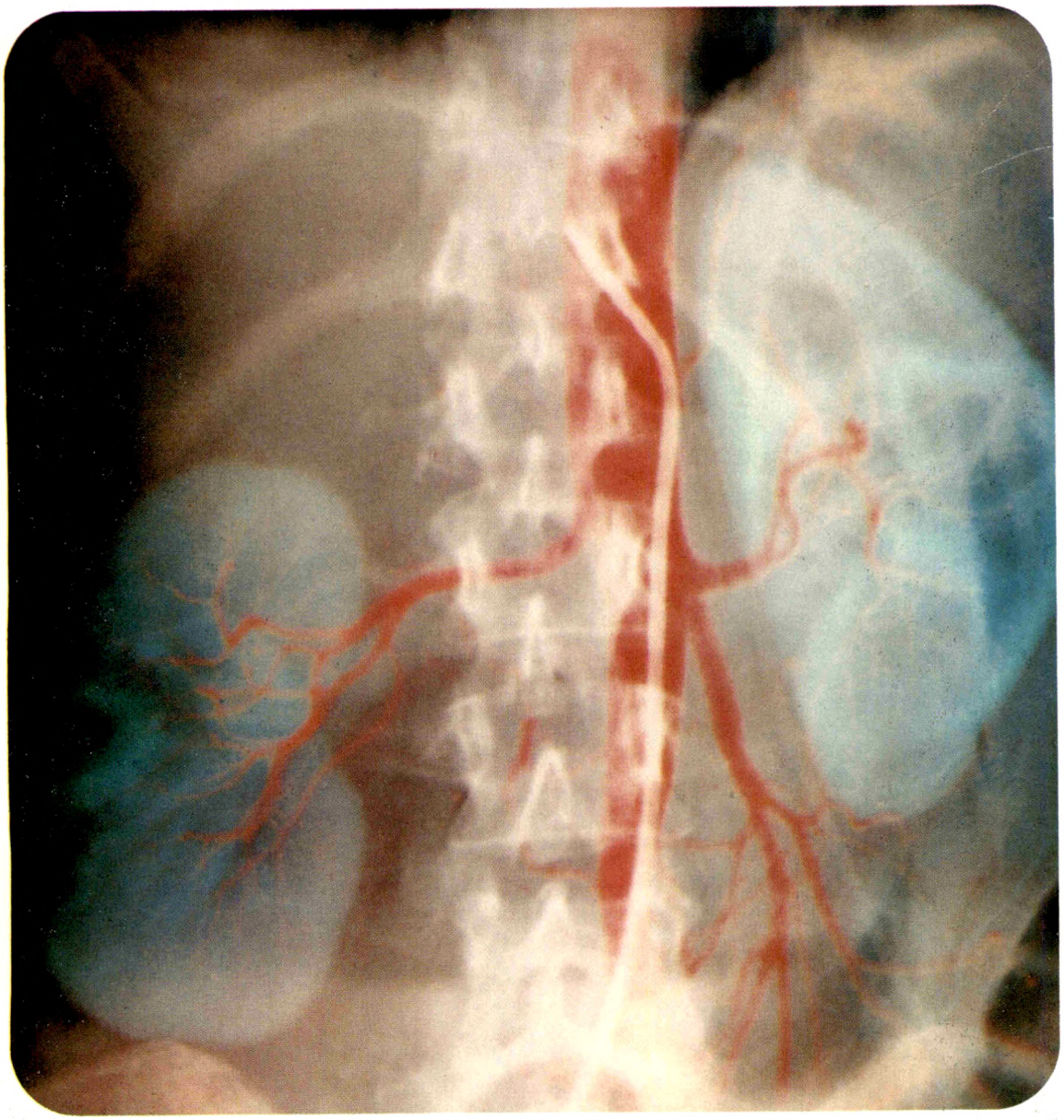
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Aortography

(percutaneous retrograde catheter technique) using Hypaque® sodium 50% as the contrast medium



The six color films illustrated, in which Hypaque was used as contrast medium, were supplied through the courtesy of Robert E. Wise, M.D. of the Lahey Clinic Foundation and New England Baptist Hospital, Boston, Mass. The technique, employing ordinary x-rays, is described in the Lahey Clinic Foundation Bulletin *14*:131, 1965.

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Hypaque® 50%

sodium

brand of **sodium diatrizoate**

Aortography with Hypaque sodium 50% may give valuable evidence in cases of renal agenesis, duplications or ectopia, or of polycystic kidney. Aortograms are also of importance in helping to demonstrate aneurysmal change or the degree of patency of the arteriosclerotic vessel, and in aiding the surgeon to determine proper surgical management if such is needed especially where a stenotic vessel is responsible for life-threatening renal hypertension. Aortograms with Hypaque 50% have provided clearly defined needed evidence of pathology prior to surgical intervention.

Excretory Urography

using Hypaque® sodium 50% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



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Excretory urography with Hypaque sodium 50% provides the detection of urinary tract lesions, without interference with functional activity, without age limit and without anesthesia—important advantages when instrumentation is undesirable.

Cerebral Arteriography

using Hypaque® sodium 50% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



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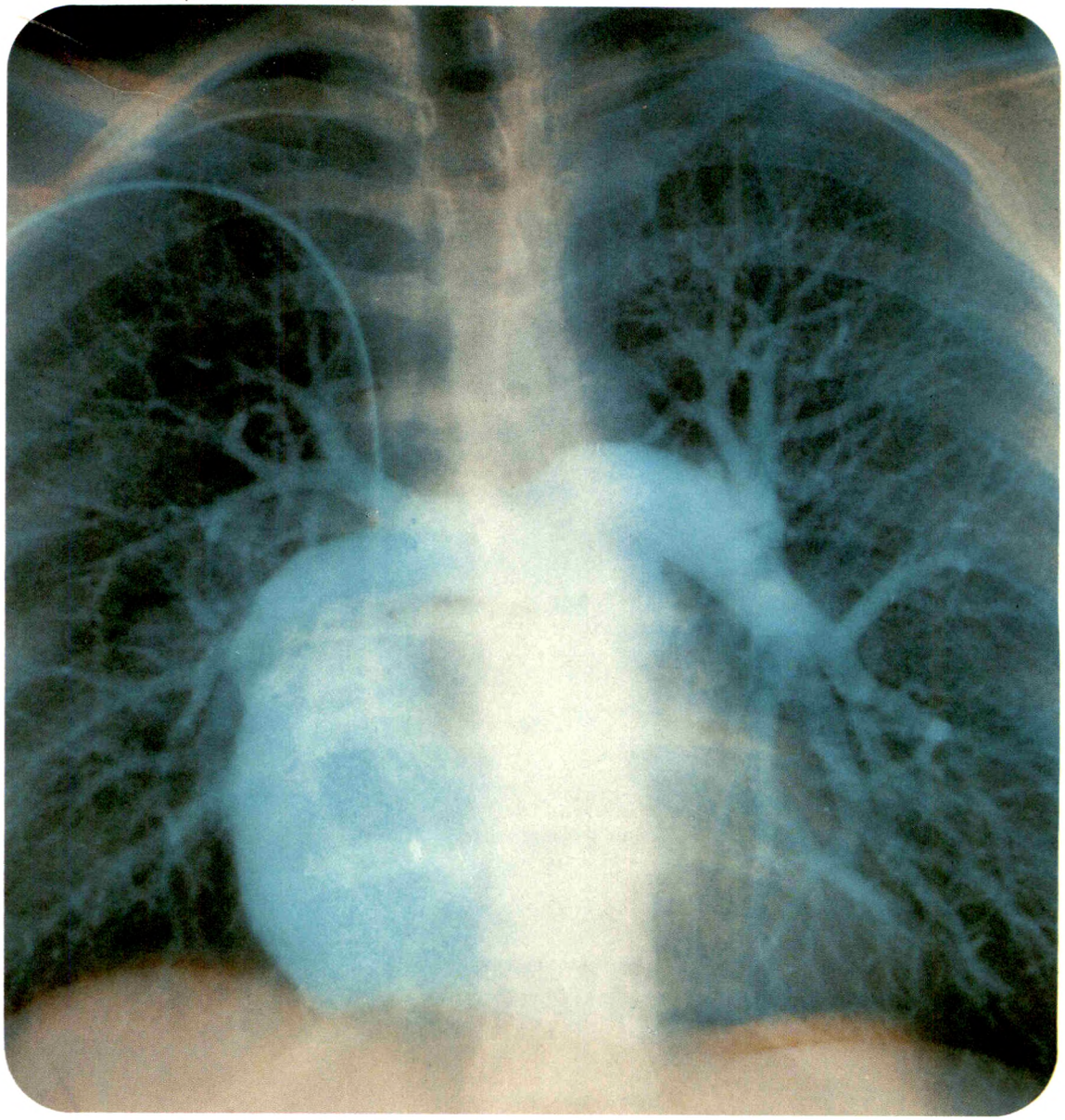
Cerebral arteriography with Hypaque sodium 50% has proved most useful in localizing and identifying intracranial lesions. Because it demonstrates both pathologic anatomy and physiology in such disorders as aneurysms, hematomas, angiomatous formations, meningiomas, glioblastoma multiforme, and other neoplasms, this procedure may provide diagnostic information frequently unobtainable by other means.

Please read the summary of prescribing information on the last pages of this unit.

Angiocardiography

using Hypaque®-M, 75% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



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Hypaque®-M, 75%

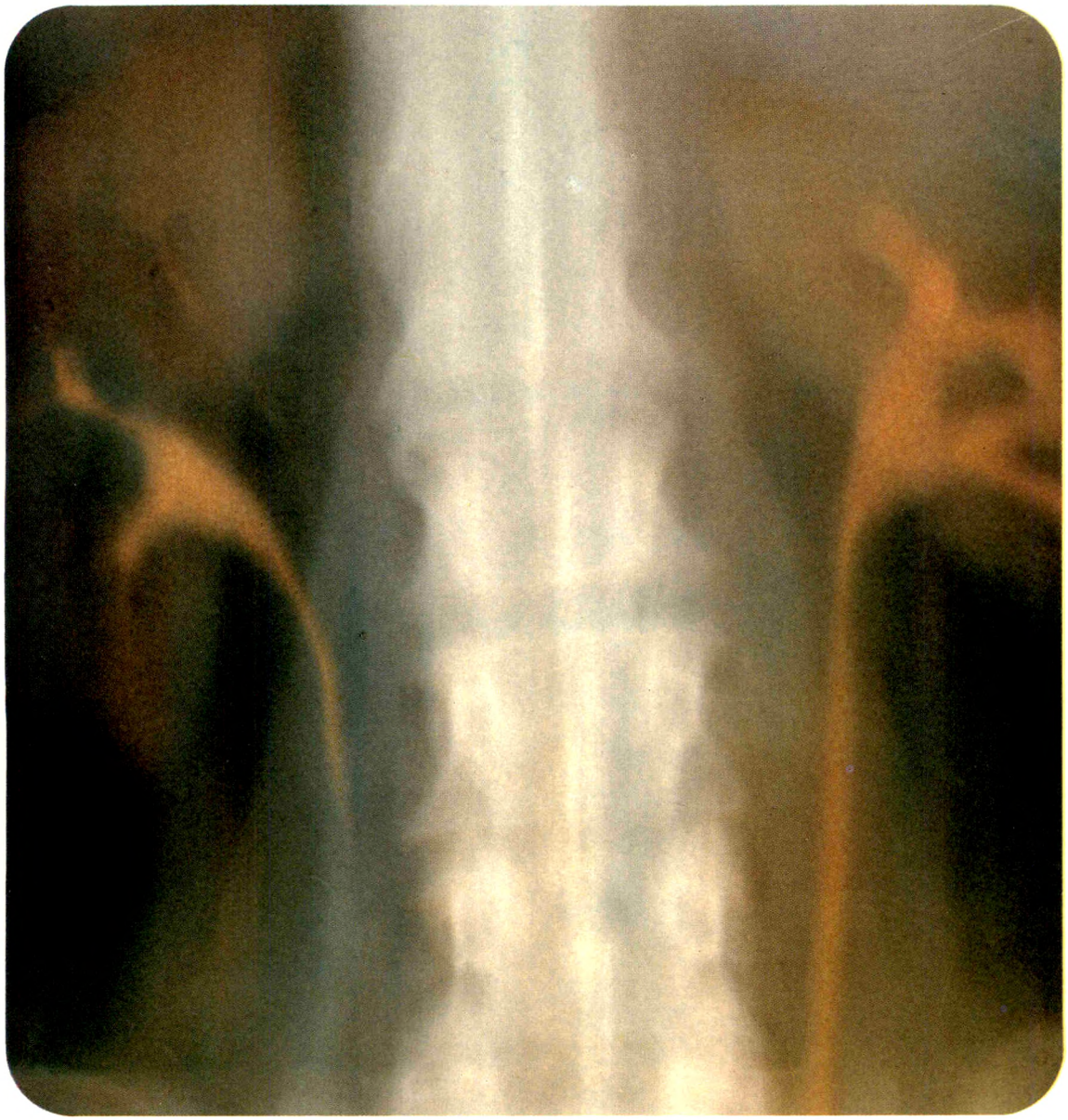
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Because the cardiac chambers and great blood vessels of the thorax can be effectively visualized with Hypaque-M 75% (90% may be used alternatively), it provides an invaluable aid in the diagnosis of a variety of congenital and acquired cardiac defects. Angiocardiography has also proved useful in the study of neoplastic and infectious diseases of the heart. Hypaque-M 75% used for this purpose is freely miscible with blood, relatively non-irritating and nontoxic in recommended dosage, and is rapidly eliminated by the kidneys.

Nephrotomography

using Hypaque®-M, 90% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



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Hypaque®-M, 90%

brand of **sodium and meglumine diatrizoates**

One of the newer methods employed to reveal the nature of renal lesions is nephrotomography —a combination of rapid intravenous nephrography and body-section radiography which provides precise delineation of renal parenchyma. Nephrotomography with Hypaque-M 90% is used primarily to differentiate renal cysts from neoplasms, but may also be indicated to distinguish renal from extrarenal masses and to demonstrate congenital anomalies of the kidney.

Please read the summary of prescribing information on the last pages of this unit

Retrograde Pyelography

using Hypaque® sodium 20% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



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Hypaque® 20%

sodium

brand of **sodium diatrizoate**

When loss of renal function or other causes result in unsatisfactory delineation of the urinary tract with intravenous techniques, retrograde pyelography with Hypaque sodium 20% solution can provide excellent anatomical details.

Please read the summary of prescribing information on the last pages of this unit.

Unsurpassed
• CONTRAST
• TOLERANCE

Pathology precisely defined
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Hypaque® sodium 50% and 20%

brand of **sodium diatrizoate**

50%, ampuls of 30 ml., vials of 20, 30 and 50 ml.
20%, bottles of 100 ml.

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Hypaque®-M, 75% and 90%

brand of **sodium and meglumine diatrizoates**

75%, vials of 20 and 50 ml.
90%, vials of 20 and 50 ml.

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Summary of Full Prescribing Information

Hypaque® Sodium 50%

brand of **sodium diatrizoate, USP**

Sterile Aqueous Injection (Weight/Volume)

Excretory Urography and Drip Infusion Pyelography

Description: Hypaque sodium is sodium 3,5-diacetamido-2,4,6-triiodobenzoate, a radiopaque medium used to delineate internal structures.

Warning: Do not use Hypaque sodium for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

General and Specific Precautions: Caution is advised in patients with a history of bronchial asthma, other allergic manifestations, or of sensitivity to iodine; these conditions represent a special risk, though not an absolute contraindication. To avoid or minimize possible allergic reactions, premedication with antihistamines may be considered. Benadryl (diphenhydramine hydrochloride) in the same syringe with Hypaque may result in precipitation. A test dose of contrast medium is not entirely reliable. Severe reactions, including fatalities, have occurred with a test dose as well as with the full diagnostic dose.

Caution is advised in patients with severe cardiovascular disease. In patients with impaired renal function and cardiovascular disease, drip infusion pyelography imposes a sudden osmotic and sodium load which can precipitate congestive heart failure. Contrast media injected into arteries or veins can promote sickling of red cells in susceptible individuals. In patients with reduced renal function, repeat of excretory or retrograde pyelography should be delayed at least 48 hours to avoid temporary suppression of urine. In preparation for excretory urography of patients with multiple myeloma, partial dehydration is not recommended, since this may predispose to the precipitation of myeloma protein in the kidney tubules. When thyroid function studies (PBI and 24-hour radioiodine uptake levels) are indicated, they should be performed *prior* to radiographic studies or several days afterwards, to avoid inaccurate results.

Hypaque sodium 50% should always be injected at body temperature.

General and Specific Adverse Reactions: Adverse reactions, usually of a minor nature, have occurred in 10-14 per cent of patients who have received Hypaque intravenously. Reactions due to *faulty technique* include hematomas and ecchymoses, following extravasation from the vein, and pyrogenic reactions. *Hemodynamic reactions* include vasodilatation with flushing, hypotension and, rarely, vein cramp or thrombophlebitis. Serious *cardiovascular reactions* include rare cases of cardiac arrhythmias (e.g., ventricular fibrillation), shock, and cardiac arrest. Transient proteinuria may occur occasionally following the injection of radiopaques and, rarely, oliguria and anuria have been reported secondary to a hypotensive reaction. *Allergic reactions* include asthmatic attacks, nasal and conjunctival symptoms, cutaneous reactions such as urticaria and, rarely, anaphylactic shock, sometimes with fatal outcome. Severe reactions may also be manifested by signs and symptoms relating to the *respiratory system* (dyspnea, cyanosis, pulmonary or laryngeal edema), or to the *nervous system* (restlessness, confusion, or convulsions). *Other reactions* include nausea, vomiting, excessive salivation, anxiety, headache, and dizziness. Infrequently, "iodism" (salivary gland swelling) from organic compounds appears two days after exposure and subsides by the sixth day. Reactions to drip infusion pyelography may not appear until some hours after the examination.

Angiography

(Peripheral Arteriography and Venography)

Precautions (See also General Precautions): Extreme caution is advised in considering peripheral arteriography in patients suspected of having thromboangiitis obliterans (Buerger's disease). Any procedure (even needling or insertion of a catheter) may induce a severe arterial and/or venous spasm. Caution is also advisable in patients with severe ischemia associated with ascending infection.

Adverse Reactions (See also General Adverse Reactions): In addition to those listed under General Adverse Reactions, are those due to arterial trauma during the procedure (i.e., needling, insertion of catheter, subintimal injection, perforation, etc.) as well as to the hypertonicity or effect of the medium; also reported are transient arterial spasm, extravasation, hemorrhage, hematoma with tamponade, injury to nerves proximal to artery, thrombosis (rare in venography; if vein is irrigated following injection), dissecting aneurysm, arteriovenous fistula, (e.g., with accidental perforation of femoral artery and vein during needling), transient leg pain from contraction of calf muscles in femoral arteriography; transient hypotension after intraarterial (brachial) injection, and brachial plexus injury with axillary artery injections.

Cerebral Angiography: Because of the special techniques required, it is recommended that Hypaque sodium be used for this purpose only by persons skilled and experienced in carrying out this procedure.

Contraindication: Carotid angiography should be avoided during the progressive period of a stroke, since this increases the risk of cerebral complications.

Precautions (See also General Precautions): Select patients for this procedure with care. Use the 50 per cent solution with caution in extreme senility (but not old age, *per se*); advanced arteriosclerosis; severe hypertension; and cardiac decompensation.

The diagnostic value of the procedure, according to many authorities, when employed early enough in locating lesions amenable to surgery, may outweigh the added risk to patients who have recently experienced cerebral embolism or thrombosis (stroke syndrome). A small number of postangiographic fatalities, including progressive thrombosis, have occurred in which the procedure did not appear to play a role.

Patients with severe cerebrovascular disease may be examined primarily by indirect methods of angiography.

Care should be exercised to avoid contaminating catheters, syringes, needles, and contrast media with glove powder or cotton fibers.

Angiography is hazardous in subarachnoid hemorrhage. In migraine, the procedure can be hazardous because of ischemic complications, particularly if performed during or soon after an attack.

Adverse Reactions (See also General Adverse Reactions): The major sources of complications are faulty technique, occlusive atherosclerotic vascular disease, repeated injections of the contrast media, and higher doses than those recommended.

Untoward reactions are mostly mild and transient, although permanent visual field defects and deaths have been reported.

Vascular reactions: flushing, vessel spasm, thrombophlebitis, and cutaneous petechiae.

Neurologic complications: transient cerebral blindness, neuromuscular disorders, convulsions, coma, hemiparesis, unilateral dysesthesias, visual field defects, aphasia, and respiratory difficulties.

Aortography

Precautions (See also General Precautions): Special caution is advised to avoid inadvertent intrathecal injection when using the translumbar technique. The incidence and severity of reactions or complications that may occur are influenced by: the care and experience with which the procedure is performed; the amount and type of medium used; the age and condition of the patient; and the premedication and anesthesia used. Since aortography is not without some danger, it should be performed only by those experienced in the technique. Wherever possible, repeated injections of the solution during a single study should be avoided.

Adverse Reactions (See also General Adverse Reactions): Renal damage and shutdown; neurologic complications such as transverse myelitis or paraplegia; cardiovascular complications such as shock, cardiac arrest or failure, coronary occlusion, arterial thrombosis, embolism, and perforation of vessels; extravasation or hemorrhage from the puncture site or retroperitoneal catheter perforation; necrosis of the intestinal wall; acute pancreatitis; deaths; diffuse cutaneous petechiae; subintimal injection and aortic dissection.

Intraosseus Venography (See General Precautions and Adverse Reactions): A general anesthetic is sometimes necessary since the method is painful. Occasionally, extravasation of the contrast medium from the needle into the soft tissue may occur.

Direct Cholangiography

Precaution (See also General Precautions): This procedure should be used with caution in the presence of acute pancreatitis, injecting no more than 5 to 10 ml. without undue pressure.

Adverse Reactions (See also General Adverse Reactions): These may be attributed to injection pressure or excessive volume of the medium, resulting in overdistention. Such pressure may produce a sensation of epigastric fullness, followed by moderate pain in the back or right upper abdominal quadrant, which will subside when injection is stopped.

Some of the medium may enter the pancreatic duct and cause a transient serum amylase elevation 6 to 18 hours later, without apparent ill effects. Pancholangitis resulting in liver abscess has been reported. Occasionally, nausea, vomiting, fever, and tachycardia have been observed.

Hysterosalpingography

Contraindications: Menstruation, active or imminent; infection in any part of the genital tract, including the external genitalia; pregnancy, known or suspected. Use not advised for six months after end of pregnancy, or 30 days after conization or curettement.

Precaution (See also General Precautions): Caution should be exercised in patients with known or suspected carcinoma to avoid possible spread of the lesion by the procedure.

Splenoportography

Precautions (See also General Precautions): Procedure should be performed with caution on patients with blood dyscrasias, a tendency to severe bleeding, or a spleen recently become tender and palpable.
Adverse Reactions (See also General Adverse Reactions): Persistent hemorrhage with hemoperitoneum has been reported, and, in some instances, hemorrhage has required splenectomy.
How Supplied: Ampuls of 30 ml., boxes of 1, 10, and 25. A 1 ml. sensitivity test ampul is furnished with each ampul. Vials of 20 and 30 ml., rubber stoppered, boxes of 1, 10, and 25. Vials of 50 ml., rubber stoppered, boxes of 1 and 10. Each vial contains sufficient excess to permit withdrawal of 1 ml. for testing sensitivity.

If the solution is chilled, crystals may form but will readily dissolve if the ampul or vial is placed in moderately hot water before use. Cool to body temperature before injecting.

Hypaque® Sodium 20%

brand of **sodium diatrizoate**

Sterile Aqueous Solution 20% (weight/volume)

Precautions: It has long been known that oliguria or anuria may rarely follow bilateral retrograde pyelography or uncomplicated cystoscopic ureteral manipulation. Various mechanisms have been proposed to explain this occurrence, such as reflex anuria, edema, and occlusion of the ureteral orifices from local trauma, pressure, manipulation, sensitivity to the radiopaque medium or to residual disinfecting antiseptic on ureteral catheters, pyelotubular backflow, transient interstitial renal edema with increased pressure, and reduced renal blood flow. Because of the possibility of acute renal failure following bilateral retrograde pyelography, some authors conclude that retrograde pyelography should be done on only one side at a time.
Side Effects: The nonirritating properties of the medium minimize the likelihood of ureteropelvic spasm; in addition, a more natural outline of the upper urinary tract is obtained because of these properties. There is also a decrease in the incidence and severity of discomfort and colic following retrograde examination. Excellent tolerance was evidenced by notably few untoward reactions. Minor side reactions, which occurred in a few patients, consisted of nausea, vomiting, excessive salivation, and sweating. There was no indication of irritation of the urinary tract mucosa that could be attributed to the medium.

With Hypaque Sodium 20 per cent, reflux into the blood stream or lymphatics (pyelovenous or pyelolymphatic backflow) as a result of undue pressure of administration is not apt to result in a generalized reaction, since intravenous injection of more than double this concentration has been well tolerated.

Hypaque®-M, 75%

brand of **sodium and meglumine diatrizoates**

Sterile Aqueous Injection 75% (weight/volume)

Caution: The 75 per cent concentration is intended primarily for angiocardiography, nephrotomography and selected cases of peripheral angiography. Hypaque sodium (brand of diatrizoate sodium) 50 per cent solution is recommended for excretory urography, cerebral angiography and most cases of peripheral angiography.
Warning: Do not use Hypaque-M, 75 per cent for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

Angiocardiography

Contraindications: Use of Hypaque-M, 75 per cent is contraindicated in patients with advanced renal destruction associated with severe uremia. Hypaque-M 75 per cent should not be used for myelography.
Precautions: 1. Caution is advised in patients with hyperthyroidism, hypertension, active tuberculosis and a history of allergy, especially to iodine. Angiocardiography and nephrotomography should be performed cautiously in patients with heart disease and circulatory failure and should not be employed in patients who are in collapse or who are critically ill or debilitated. A renal function test is advisable before administration of the 75 per cent solution.

2. Prior to the examination, the patient may be tested for sensitivity to the radiopaque medium. (See Side Effects and Sensitivity Tests.) Patients who show an idiosyncrasy should not be given the drug.

3. Premedication with a barbiturate is advisable if the patient is extremely nervous. Demerol (brand of meperidine), chlorpromazine and antihistamines have also been recommended for premedication. Such antihistamines as chlorpheniramine maleate or tripelennamine hydrochloride may be administered about 30 minutes before injection of the radiopaque medium or may be combined with it in a single injection. Many authorities recommend general anesthesia for small children and uncooperative patients.

4. Facilities for resuscitation including a mask with a breathing bag and pure oxygen should be available for immediate administration in case of severe reaction.

5. The sensations to be experienced should be described to the patient in order to allay apprehension before injection and to prevent excitement afterward.

6. To facilitate venipuncture, the needle should be sharp, the arm extended and the vein large and fully distended.

7. The syringe must be scrupulously clean in order to prevent sticking of the plunger during injection.

8. If crystals form, the solution should be warmed and agitated until they have redissolved. Injection should be made only when the solution is clear and is at a temperature of approximately 37.5° C.

9. Injection should be made only when there is free communication between needle and vein. When in doubt, another vein should be tried or the test postponed. Vein and needle should be watched during injection to prevent displacement of the needle or overdistention of the vein. If extravasation occurs, the injection should be stopped and a quantity of physiologic saline solution administered through the needle to dilute the radiopaque medium and to lessen the possibility of irritation.

10. Some authorities advise that repeated injections should not be given in close sequence and, if possible, should be avoided.
Side Effects and Sensitivity Tests: As with other radiopaque mediums, certain side effects occasionally may be encountered, although the 75 per cent solution has been well tolerated when given in recommended dosages. Serious complications following angiocardiography may be due to varying and perhaps unrelated factors. Symptoms may be due to the speed of injection and the anxiety and psychic stress associated with the examination, as well as to the material injected. Side effects will usually be minor and transient and may include a sensation of warmth and flushing, nausea, vein cramp, mild tachycardia, metallic or acid taste, tightness in the chest, headache, cough or urticaria. Delayed reactions may occur. Venous thrombosis has not been observed in patients receiving the 75 per cent solution, but as with any rapidly injected hypertonic solution, the possibility of this complication exists.

Angiocardiographic contrast mediums may produce symptoms of an anaphylactic nature in sensitive persons. Patients should be observed carefully during injection, as serious reactions including fatalities have occurred with most mediums. Since it is believed that reactions to intravenously administered organic iodine radiopaque agents are more likely to develop in patients with allergic diathesis, special care is advisable in persons with a history of asthma or other allergic manifestations.

Various methods have been advocated to detect sensitivity to contrast mediums, particularly conjunctival, oral, intradermal and intravenous testing. Conjunctival, oral and intradermal tests are not reliable, since reactions to them are generally caused by direct local vascular effect. Occasionally a severe reaction in the eye has followed a conjunctival test. An intravenous test is more likely to demonstrate sensitivity, although a negative reaction does not necessarily rule out the possibility. A small dose of 0.5 to 1 ml. is slowly injected intravenously over a period of one minute, followed by a period of observation sufficiently long to detect delayed reactions. Although allergic reactions generally occur quickly, occasionally they may not be manifested for 10 or even 15 minutes.

Warning signs and symptoms of possible intolerance or allergy include respiratory difficulty (wheezing, dyspnea or sensation of suffocation or tightness in the throat or chest), sneezing, itching, urticaria, nausea or vomiting and fainting.
Treatment of Reactions: (Same as with Hypaque Sodium 50%)

Nephrotomography

Contraindications, Precautions, Side Effects and Treatment of Reactions: See Angiocardiography.

Hypaque®-M, 90%

brand of **sodium and meglumine diatrizoates**

Sterile Aqueous Injection 90% (weight/volume)

Caution: Hypaque-M, 90 per cent is intended primarily for angiocardiography, nephrotomography, hysterosalpingography and selected cases of peripheral angiography. Hypaque sodium

Hypaque®-M, 90%
brand of **sodium and meglumine diatrizoates (cont.)**

50 per cent solution is recommended for excretory urography, cerebral angiography and most cases of peripheral angiography.
Warning: Do not use Hypaque-M, 90 per cent for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

Angiocardiography

Contraindications: Use of Hypaque-M, 90 per cent is contraindicated in patients with advanced renal destruction associated with severe uremia. Hypaque-M, 90 per cent should not be used for myelography.
Precautions: 1. Caution is advised in patients with hyperthyroidism, hypertension, active tuberculosis and a history of allergy, especially to iodine. Angiocardiography and nephrotomography should be performed cautiously in patients with heart disease and circulatory failure and should not be employed in patients who are in collapse or who are critically ill or debilitated. A renal function test is advisable before administration of Hypaque-M, 90 per cent.

2. Prior to the examination, the patient may be tested for sensitivity to Hypaque-M, 90 per cent. (See Side Effects and Sensitivity Tests.) Patients who show an idiosyncrasy to Hypaque-M, 90 per cent should not be given the drug.

3. Premedication with a barbiturate is advisable if the patient is extremely nervous. Demerol (brand of meperidine), chlorpromazine and antihistamines have also been recommended for premedication. Such antihistamines as chlorpheniramine maleate or tripelennamine hydrochloride may be administered about thirty minutes before injection of Hypaque-M, 90 per cent or may be combined with it in a single injection. Many authorities recommend general anesthesia for small children and uncooperative patients.

4. Facilities for resuscitation including a mask with a breathing bag and pure oxygen should be available for immediate administration in case of severe reaction.

5. The sensations to be experienced should be described to the patient in order to allay apprehension before injection and to prevent excitement afterward.

6. To facilitate venipuncture, the needle should be sharp, the arm extended and the vein large and fully distended.

7. The syringe must be scrupulously clean in order to prevent sticking of the plunger during injection.

8. Hypaque-M, 90 per cent should be warmed and agitated until all suspended crystals have redissolved. Injection should be made only when the solution is clear and is at a temperature of approximately 37.5°C.

9. Injection should be made only when there is free communication between needle and vein. When in doubt, another vein should be tried or the test postponed. Vein and needle should be watched during injection to prevent displacement of the needle or overdistention of the vein. If extravasation occurs, the injection should be stopped and a quantity of physiologic saline solution administered through the needle to dilute the Hypaque-M, 90 per cent and to lessen the possibility of irritation.

10. Some authorities advise that repeated injections should not be given in close sequence and, if possible, should be avoided.

Hypaque®-M, 90%
brand of **sodium and meglumine diatrizoates (cont.)**

Side Effects and Sensitivity Tests: Serious complications following angiocardiography may be due to varying and perhaps unrelated factors. Symptoms may be due to the speed of injection and the anxiety and psychic stress associated with the examination, as well as to the material injected. Side effects noted with Hypaque-M, 90 per cent were usually of a minor and transient nature and included a sensation of flushing or warmth, nausea, vein cramp, mild tachycardia, metallic or acid taste, tightness in the chest, headache, cough or urticaria. Delayed reactions may occur. Venous thrombosis has been observed in patients following the percutaneous insertion of the injection needle. This complication may be anticipated, however, when concentrated hypertonic solutions are injected rapidly. In skilled hands, the administration of Hypaque-M, 90 per cent is attended by comparatively few untoward reactions.

Angiocardiographic contrast mediums may produce symptoms of an anaphylactic nature in sensitive persons. Patients should be observed carefully during injection, as serious reactions including fatalities have occurred with most mediums. Since it is believed that reactions to intravenously administered organic iodine radiopaque agents are more likely to develop in patients with allergic diathesis, special care is advisable in persons with a history of asthma or other allergic manifestations.

Various methods have been advocated to detect sensitivity to contrast mediums, particularly conjunctival, oral, intradermal and intravenous testing. Conjunctival, oral and intradermal tests are not reliable, since reactions to them are generally caused by a direct local vascular effect. Occasionally a severe reaction in the eye has followed a conjunctival test. An intravenous test is more likely to demonstrate sensitivity, although a negative reaction does not necessarily rule out the possibility. A small dose of from 0.5 to 1 ml. is slowly injected intravenously over a period of one minute, followed by a period of observation sufficiently long to detect delayed reactions. Although allergic reactions generally occur quickly, occasionally they may not be manifested for ten or even fifteen minutes.

Warning signs and symptoms of possible intolerance or allergy include respiratory difficulty (wheezing, dyspnea or sensation of suffocation or tightness in the throat or chest), sneezing, itching, urticaria, nausea or vomiting and fainting.
Treatment of Reactions: (Same as with Hypaque Sodium 50%)

Nephrotomography

Contraindications, Precautions, Side Effects and Treatment of Reactions: See Angiocardiography.

Hysterosalpingography

Contraindications: The procedure should not be performed during the menstrual period or when menstrual flow is imminent, nor should it be performed when infection is present in any portion of the genital tract, including the external genitalia. The procedure is also contraindicated for pregnant women or for those in whom pregnancy is suspected. Its use is not advised for six months after termination of pregnancy, or for thirty days after conization or curettement.
Precautions: In patients with carcinoma or in those in whom the condition is suspected, caution should be exercised to avoid possible spread of the lesion by the procedure.

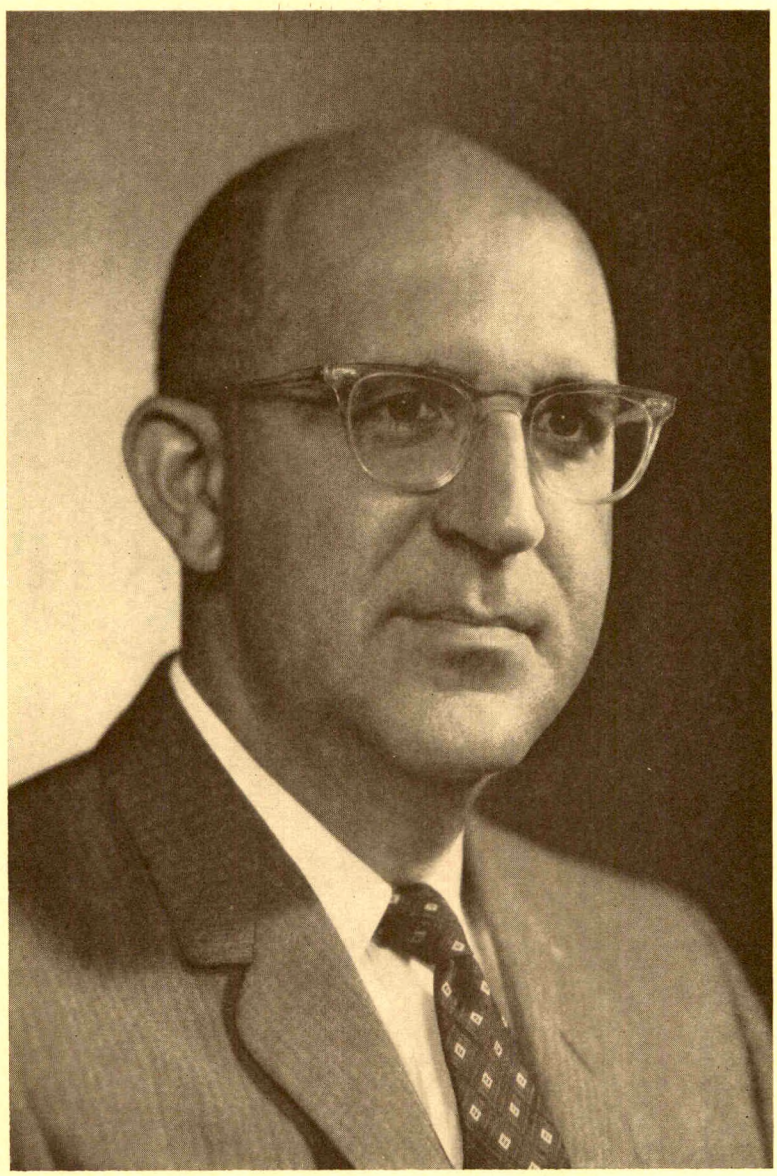
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JUAN M. TAVERAS, M.D.
Caldwell Lecturer, 1968

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MULTIPLE PROGRESSIVE INTRACRANIAL ARTERIAL OCCLUSIONS: A SYNDROME OF CHILDREN AND YOUNG ADULTS*

CALDWELL LECTURE, 1968

By JUAN M. TAVERAS, M.D.
ST. LOUIS, MISSOURI

INTRACRANIAL arterial occlusive lesions leading to what is generally known as the "stroke syndrome" are among the most common conditions in medicine and are most often encountered in the 6th and 7th decades of life or later. It is well known that in the earlier decades of life a stroke may be produced by lesions such as bleeding congenital saccular aneurysms or spontaneous intracranial hemorrhage produced by rupture of small vascular malformations. Arterial embolization is another cause of stroke in the younger group and is usually associated with conditions that lead to intravascular coagulation or to the formation of free fragments of inflammatory granulomatous processes in the arterial blood stream. What is less known is that thrombotic arterial occlusions occur not infrequently in childhood and in the earlier decades of life.

Hemiplegias encountered during infancy or childhood are usually due to occlusion of the internal carotid artery or major branches of the middle cerebral artery secondary to embolism, infection, trauma or to a localized arterial lesion. Very frequently, the relationship of the occlusive lesion with an infectious disease process is not very clearly established. Before the advent of cerebral angiography as a routine diagnostic procedure in neurologic patients, the pathogenesis of infantile and childhood hemiplegias was open to discussion. Since the introduction of cerebral angiography as a routine procedure, however, obstruction of either the supraclinoid internal carotid artery or the middle cerebral artery or major branches of the middle cerebral artery is usually demonstrated in the early stages. In late infantile hemiplegias with significant residual sequelae of spastic hemiparesis, angiography usually shows changes which indicate an old vascular occlusion with recanalization of the occluded major arteries.

* Presented at the Sixty-ninth Annual Meeting of the American Roentgen Ray Society, New Orleans, Louisiana, October 1–4, 1968.
From the Edward Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, Missouri.

The disease process to be discussed here is not the usual hemiplegia encountered in children or young adults, but one in which the intracranial portions of both internal carotid arteries, both middle and both anterior cerebral arteries, and sometimes the basilar and trunk of posterior cerebral arteries, become occluded.

Bilateral occlusion of the internal carotid arteries at the bifurcation of the common carotid arteries in the later decades of life is not rare.[3,12,15,16,22,41] The occlusion in those cases, however, is in the cervical segment of the internal carotid artery and only occasionally is it found in the distal portion of the internal carotid artery without evidence of atherosclerotic narrowing in the proximal portion.

MATERIAL

The material consists of 10 cases which I consider to fit the criteria of the syndrome under consideration. At least 8 other cases have been seen but, because of incomplete angiographic study or because of other questionable features, they are not included here.

REPORT OF CASES

CASE 1. M. G., a 31 year old woman was admitted to the Neurological Institute of New York with weakness of the left arm for $2\frac{1}{2}$ months. This episode had started when she suddenly fell to the floor; upon getting up, she noticed weakness of the left extremities. Nine months prior to admission, the patient had complained of pain in the left buttock which necessitated treatment by traction for 2 weeks. Subsequently, the husband noted that the left corner of the patient's mouth drooped and she had a vacant stare at times. She gradually became confused, disoriented, had hallucinations, and was placed in a psychiatric institution where a diagnosis of schizophrenia was made. She was discharged after 1 month, improved, and was described as having a persistent left facial drooping. At home she was withdrawn and forgetful. Sometime later while shopping with her husband, she became suddenly limp and slightly confused. Paralysis of the left arm and weakness of the left leg were noted at that time. One week later, the patient had another episode in which she lost consciousness and remained so for 1 to 2 days. She was in bed for 3 weeks with gradual return of strength. General physical examination on admission was essentially negative.

Neurologic examination. This revealed primarily a partial left spastic hemiplegia without signs of increased intracranial pressure.

Laboratory data. Routine laboratory studies were all negative. The electrocardiographic report indicated that the T-waves were abnormal, but of no specific pattern. The EEG showed some *right* sided signs and bursts of high voltage slow activity in response to hyperventilation but was considered as technically not fully satisfactory. The patient was incontinent during the test.

Roentgenologic examination (1953). The skull roentgenograms were negative. A right carotid angiogram on February 10, 1953 (Fig. 1*A*) demonstrated the presence of occlusion of the proximal middle cerebral vessels at the bifurcation of the trunk of this artery. There was filling of many small vessels in the region of the basal ganglia and extending into the upper brain stem area. At that time, it was felt that this could represent a malignant tumor in the region of the thalamus because it was not fully appreciated that the filling of the

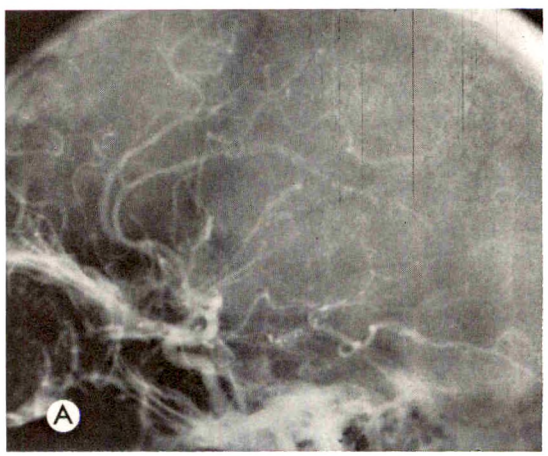


FIG. 1. Case 1. (*A*) Right carotid angiogram obtained on February 10, 1953. The lateral view at 1 second shows good filling of the internal carotid artery and of the anterior cerebral artery and its branches. The middle cerebral artery is incompletely filled at this time due to partial occlusion of the middle cerebral artery. There are fine vessels behind and above the sella turcica region. Later in the series, all of the branches filled.

distal portion of the middle cerebral artery took place by way of collateral circulation. Ventriculography was performed which failed to demonstrate any shift or deformity of the third ventricle. There was enlargement of the right lateral ventricle and gas in the region of the sylvian fissure on the right side in increased amounts suggesting atrophy.

Clinical course. The patient was discharged to be followed in the clinic. A year and one-half later the patient had 2 attacks of confusion and weakness of the *left side* lasting 2 days. Four years after the initial hospital admission, she had 2 seizures and was seen in the clinic at which time some weakness of the *right side* with increased deep tendon reflexes and questionable Babinski sign on the right side was described. During the interval, she had an intermittent motor speech defect, persistent right sided headaches, and little change in her neurologic picture but was getting along rather well otherwise, performing all of her domestic tasks. She was readmitted 7 years after the original episode for further study and re-evaluation. Her neurologic status was essentially unchanged. At that time, there was a left spastic hemiparesis, moderate atrophy of the left hand with flexion contractures of the fingers. There was increased tone throughout the right side. The left hemiparesis was considered more marked in the upper than the lower extremity. The speech showed a mild global aphasia. The reflexes showed a left reflex preponderance, bilateral Hoffmann sign, but no abnormal plantar responses. The laboratory examinations were normal. The electroencephalogram showed a prominent fairly continuous left temporal abnormality with some left frontal and rarely left parietal involvement. The right side was mostly normal with occasional atypical paroxysmal activity in the right frontal region.

Roentgenologic examination (1961). The skull now showed large tortuous right and left middle meningeal artery grooves which were seen in the original roentgenograms but were found to be less enlarged 4 years earlier (Fig. 1, *B* and *C*). Right and left common carotid angiography was carried out and showed complete occlusion of the internal carotid artery in the supraclinoid portion on the right side (Fig. 1, *G* and *H*). On the left side, the occlusion was at the trunk of the middle cerebral artery at its origin and at the trunk of the anterior cerebral artery slightly more distally (Fig. 1, *D–F*). Filling of the distal portion of the anterior, middle, and posterior cerebral artery territories took place by way of considerably dilated perforating branches in the basal ganglia region, and by way of transdural anastomoses (*rete mirabile*) between branches of the external carotid artery (mostly middle meningeal and other meningeal arteries) and the superficial branches of the middle, anterior, and posterior cerebral arteries. The fact that the posterior cerebral and superior cerebellar arteries filled by this route indicates that the basilar artery was also occluded, but at the time of these angiograms it was decided not to subject the patient to further arteriography. Actually, upon review of the original angiogram obtained 7 years previously, the appearance

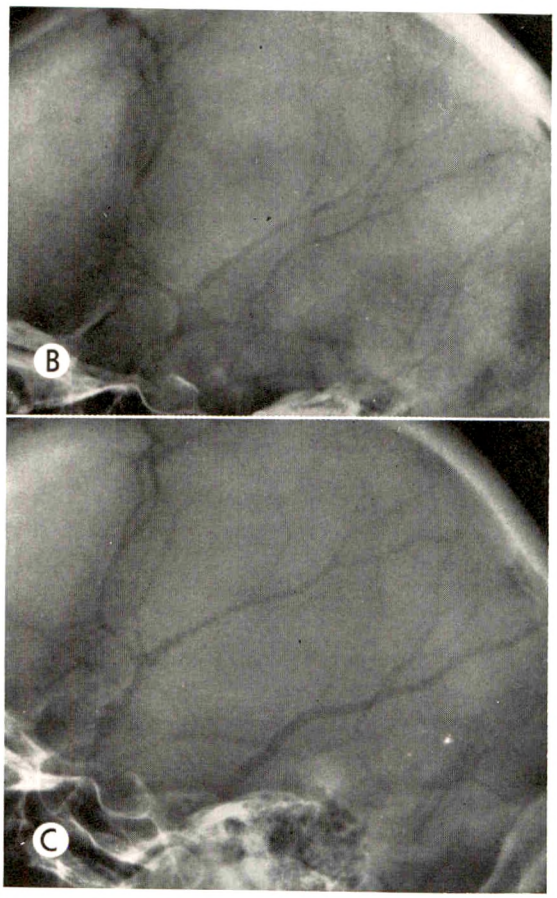


Fig. 1. (*B*) Plain roentgenogram in the lateral view made in 1957 shows enlargement of the middle meningeal artery grooves on both sides. (*C*) Plain lateral skull roentgenogram made in 1961 shows considerable further increase in the size of the middle meningeal artery grooves.

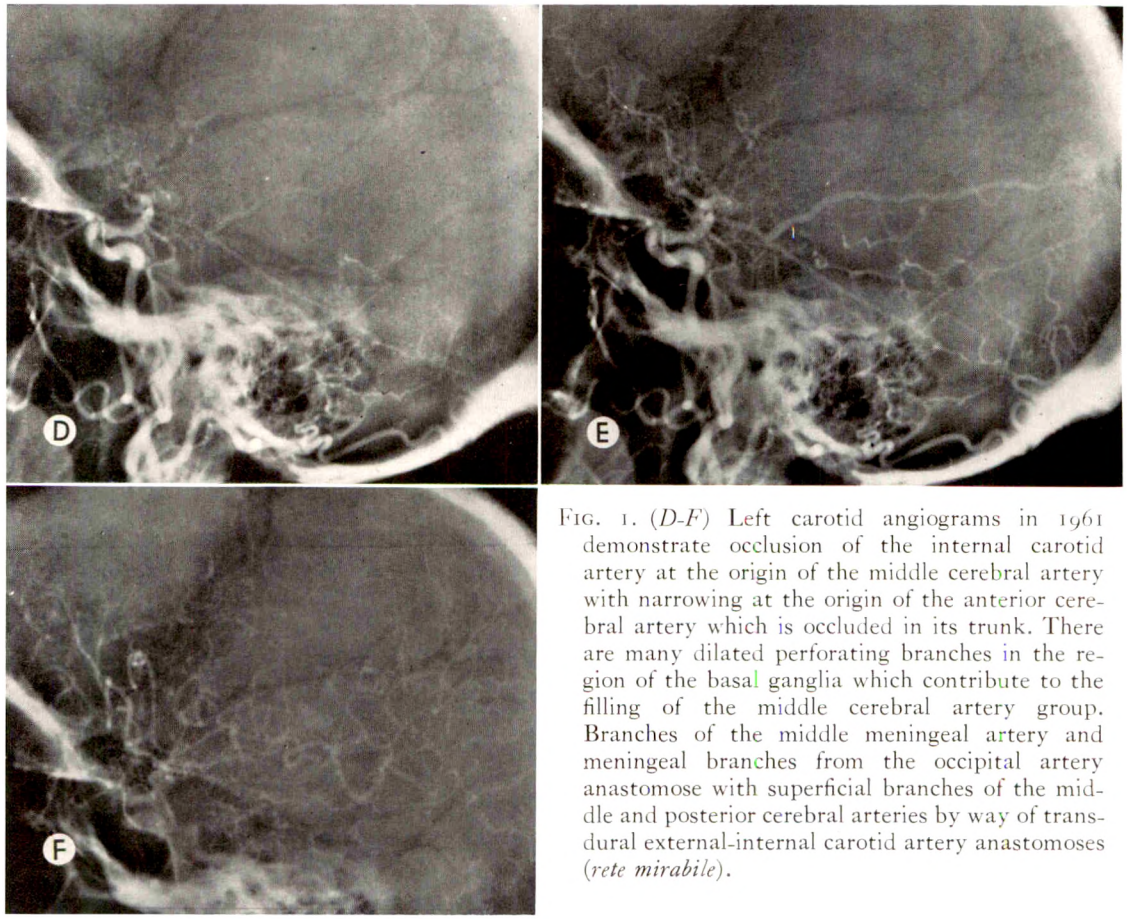


FIG. 1. (*D-F*) Left carotid angiograms in 1961 demonstrate occlusion of the internal carotid artery at the origin of the middle cerebral artery with narrowing at the origin of the anterior cerebral artery which is occluded in its trunk. There are many dilated perforating branches in the region of the basal ganglia which contribute to the filling of the middle cerebral artery group. Branches of the middle meningeal artery and meningeal branches from the occipital artery anastomose with superficial branches of the middle and posterior cerebral arteries by way of transdural external-internal carotid artery anastomoses (*rete mirabile*).

suggests occlusion of the basilar artery at that time because of the presence of unusual increased vascularity overlying the brain stem region filled by way of the carotid injection.

In summary, this is a 31 year old woman who had onset of left hemiplegia and prior to that had occasional attacks of staring and loss of consciousness. She was treated for what was thought to be a psychiatric condition because of confusion and hallucinations. On the first admission, she had partial occlusion of middle cerebral artery and patent anterior cerebral artery. Repeat angiography 7 years later showed that now both internal carotid arteries were occluded at the origin of the anterior and middle cerebral arteries with considerably increased collateral flow by way of deep anastomotic vessels and by way of transdural external-internal carotid anastomoses. In the intervening 8 years, she had had some symptoms suggestive of bilateral involvement. Basilar artery occlusion was probably also present but was not investigated. There were no other signs of arterial disease elsewhere in the body.

CASE II. T. B., a 24 year old man was admitted to Cincinnati V. A. Hospital because of vomiting, weakness, and headaches. Upon admission, he was disoriented. A spinal tap showed bloody spinal fluid. The symptoms improved steadily and he was finally discharged and sent back to military duty some $3\frac{1}{2}$ months later. Several arteriographic studies were performed during this admission. A right superficial temporal artery biopsy was done at that time which was found to be normal, showing no evidence of arteritis. He continued to have headaches, however, and he felt that these were related to the temporal artery biopsy and did not attach too much significance to them. With activity, there was more headache and 1 month after returning to military service he had nausea and vomiting accompanied by more headaches.

Neurologic examination. This had been es-

sentially negative and at this time no significant abnormal findings were noted. He had a right lid ptosis and poor performance of the serial sevens. He had visual acuity of 20/100 in the right eye, but by history this was a long-term problem. During this time, the patient complained frequently of headaches. Approximately $3\frac{1}{2}$ years later, he was admitted because of frequent intractable headaches. In the meantime, the patient was gainfully employed and aside from the headaches was doing well. His neurologic and physical examination was unremarkable. Pneumoencephalography was carried out at that time. In the interim, he had also undergone cerebral angiography twice.

Roentgenologic examination. Left carotid angiography performed on January 11, 1965, 9 days after onset showed narrowing of the supraclinoid portion of the internal carotid artery and good filling of the anterior cerebral artery trunk and of the middle cerebral artery on this side. There was an area of narrowing above the anterior communicating artery (Fig. 2, *A*, *B*, and *C*). It was noted in the frontal projection that there was filling of branches of the anterior cerebral artery on the right side. This was suspected as being due to occlusion of the right anterior cerebral artery. Right carotid angiography was not performed at this time.

Repeat left carotid angiography on January 21, 1965 (Fig. 2, *D* and *E*), showed that there was almost complete occlusion of the anterior cerebral artery distal to the anterior communicating artery and considerable narrowing of the middle cerebral artery trunk with dilatation of the deep perforating branches in the basal ganglia region. At this time, many small ill-defined arterial branches were seen in the region of the corpus callosum which were felt to represent a collateral pathway for filling of the right pericallosal artery from the left.

Right carotid angiography (Fig. 2, *F* and *G*) was now performed and demonstrated complete occlusion of the internal carotid artery in the region of the bifurcation of this vessel with filling of only the middle cerebral branches by way of considerably dilated perforating branches arising from the anterior choroidal artery, distal internal carotid artery, and possibly posterior communicating artery. The anterior cerebral artery was not seen to fill by this route.

Right brachial angiography on August 8, 1966 (Fig. 2*J*), demonstrated a normal basilar

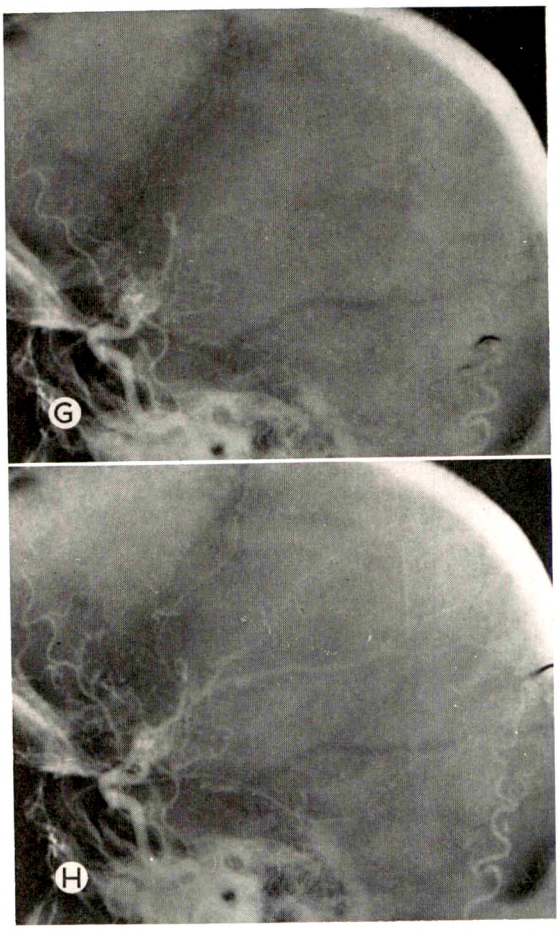


Fig. 1. (*G* and *H*) Right carotid angiograms demonstrate occlusion of the internal carotid artery in its supraclinoid portion and a large network of vessels arising from the occluded internal carotid artery in the basal ganglia region. There are also transdural external-internal carotid anastomotic pathways demonstrated on this side.

artery which filled only the right posterior cerebral artery well. The left posterior cerebral artery was very faintly visualized. There was slight filling of the right internal carotid artery which was occluded at the same site as previously seen; many dilated thin vessels in the region of the basal ganglia and on the medial side of the hemisphere on the right were again visible. It appears that the angiographic picture of the right carotid artery was unchanged, although visualization at this time was not optimal.

Repeat left carotid angiography on August 9, 1966 (Fig. 2, *H* and *I*), showed that the internal carotid artery and the anterior and middle

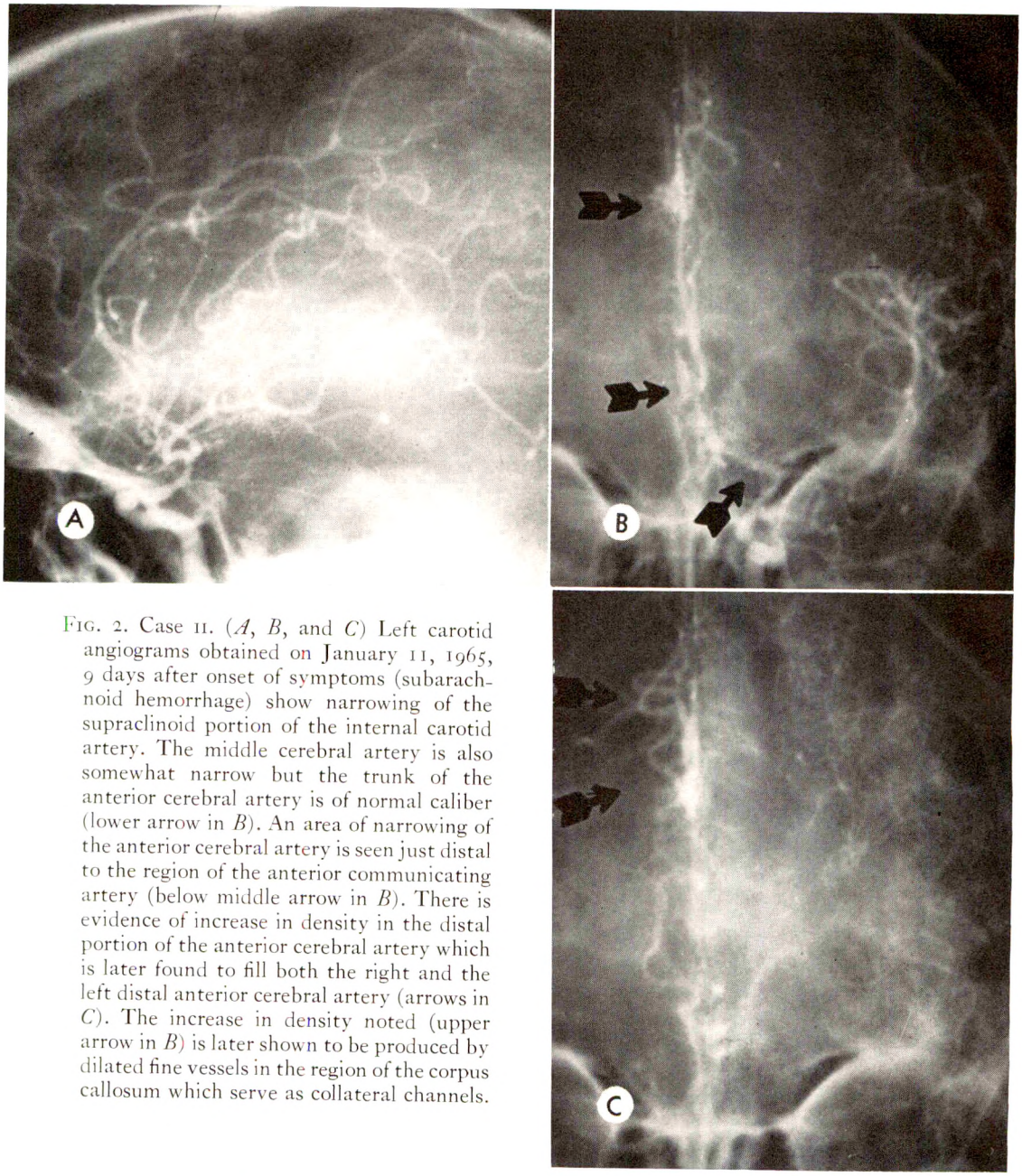


Fig. 2. Case 11. (*A*, *B*, and *C*) Left carotid angiograms obtained on January 11, 1965, 9 days after onset of symptoms (subarachnoid hemorrhage) show narrowing of the supraclinoid portion of the internal carotid artery. The middle cerebral artery is also somewhat narrow but the trunk of the anterior cerebral artery is of normal caliber (lower arrow in *B*). An area of narrowing of the anterior cerebral artery is seen just distal to the region of the anterior communicating artery (below middle arrow in *B*). There is evidence of increase in density in the distal portion of the anterior cerebral artery which is later found to fill both the right and the left distal anterior cerebral artery (arrows in *C*). The increase in density noted (upper arrow in *B*) is later shown to be produced by dilated fine vessels in the region of the corpus callosum which serve as collateral channels.

cerebral arteries were normal except for an area of narrowing in the proximal pericallosal artery. Very little of the right anterior cerebral artery filled by way of the anterior communicating artery, but there were many small dilated thin vessels in the region of the corpus callosum indicating the presence of collateral pathways in this region.

Pneumoencephalography on May 28, 1968, demonstrated mild ventricular dilatation bilaterally, slightly more marked on the left, and was otherwise normal (Fig. 2*K*).

In summary, this is a 24 year old man who had repeated headaches over a period of some years, which at one time were thought to be due to a subarachnoid hemorrhage with essentially negative neurologic findings. The angiograms revealed occlusion of the right internal carotid artery with numerous deep collateral channels, and almost complete occlusion of the left ante-

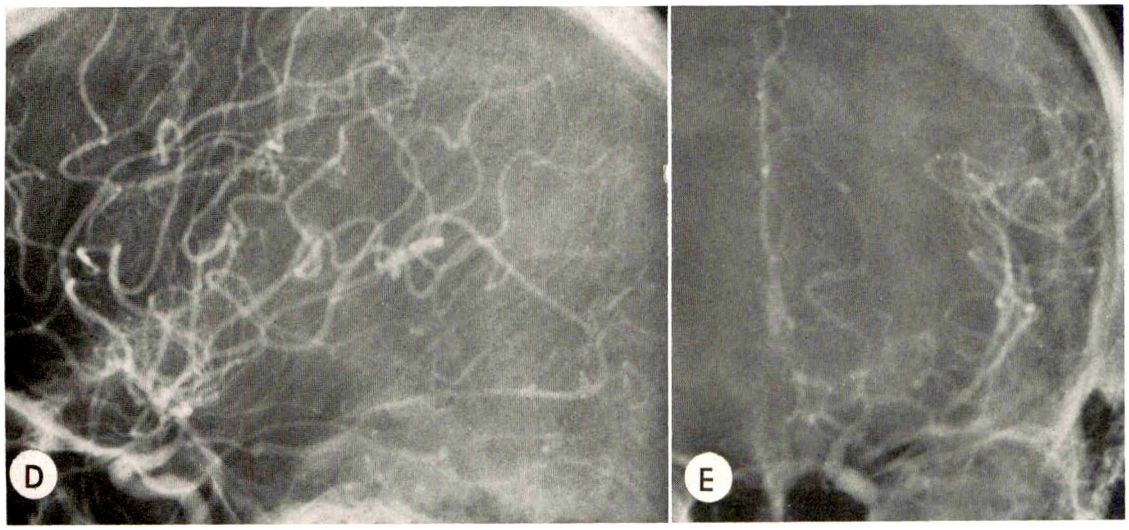


Fig. 2. (*D* and *E*) Repeat left sided angiography *ten days later* (January 21, 1965) shows the persistent narrowing of the supraclinoid portion of the internal carotid artery and of the middle cerebral artery. The anterior cerebral artery at this time shows considerably more narrowing and there appears to be an almost complete interruption of the anterior cerebral artery above the anterior communicating artery. Filling may take place by way of fine collaterals. The distal middle and anterior cerebral artery branches are normal in appearance and so is the left posterior cerebral artery.

rior cerebral artery, with enlarged collateral channels between pericallosal arteries in the region of the corpus callosum. The angiographic appearance of the vessels on the left side improved on examinations performed 4 months and 1½ years later. This raises the question as to whether arterial spasm on the left side was not contributing to the narrowing of the anterior and middle cerebral artery trunk in the second examination. Against spasm is the fact that the first examination did not show significant narrowing of some of the vessels. Pneumoencephal-

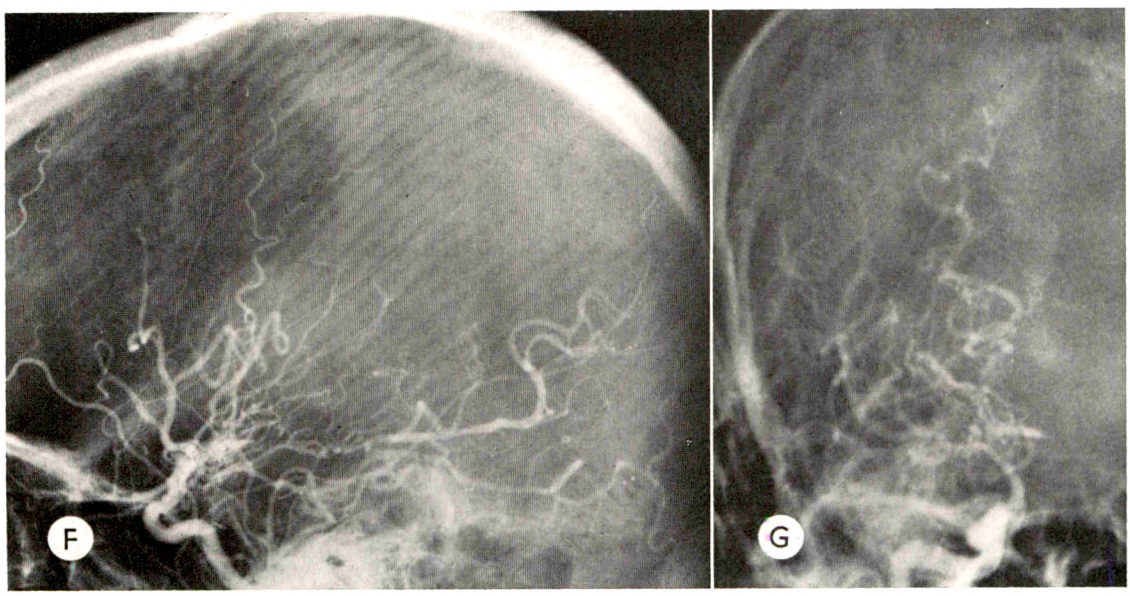


Fig. 2. (*F* and *G*) Right common carotid angiograms on January 21, 1965, show occlusion of the internal carotid artery in the supraclinoid portion with numerous fine network collaterals in the region of the basal ganglia which are obviously acting as collateral pathways. There is also *involvement of the proximal posterior cerebral artery* as shown in *G*.

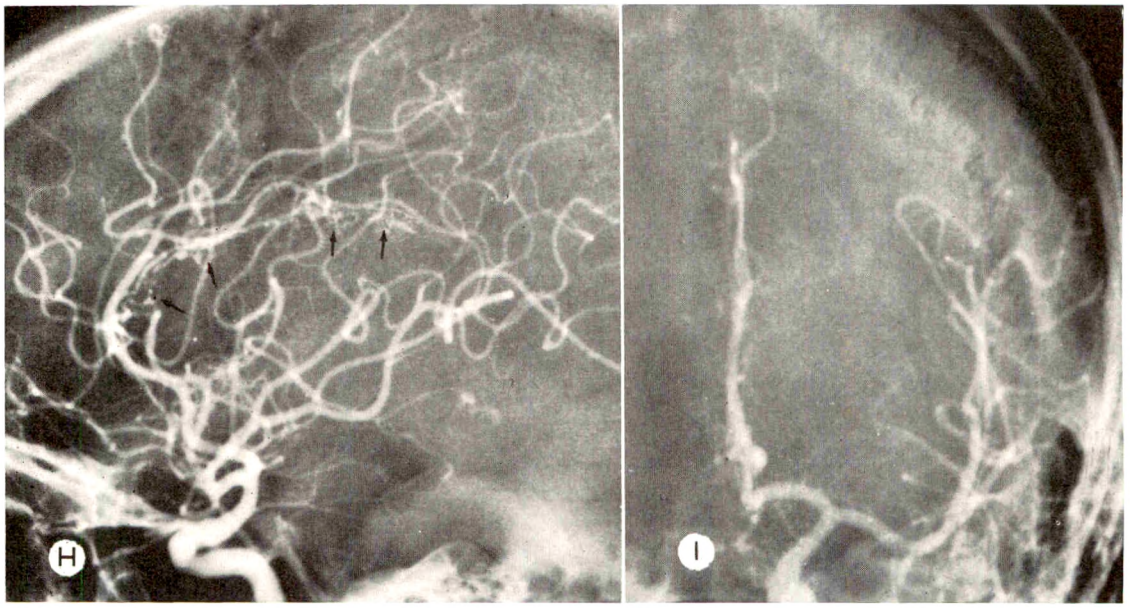


FIG. 2. (*H* and *I*) Repeat left carotid angiography on August 9, 1966, now shows a nearly complete return to normal of the internal carotid artery system. Only slight narrowing of the anterior cerebral artery segment just distal to the anterior communicating artery is present. The dilated fine collaterals in the region of the corpus callosum are still visible (arrows).

ography in 1968 showed greater ventricular enlargement of the left side, the one where the vascular changes regressed.

CASE III. T.L.B. is a 3 year old girl admitted to Barnes Hospital of St. Louis because she had had 4 episodes of alternating hemiparesis in the preceding 2 years, first on the right side lasting for a few hours, 2 weeks later on the left side also lasting for a few hours. Some months later she had jerking movements and twitching on the left side. At that time she was placed on phenobarbital medication and had no further difficulty. Ten days before admission she developed drooping of the right eyelid followed by a left hemiparesis. The symptoms persisted and were present at the time of admission. The physical examination was normal and the neurologic examination was negative aside from the hemiparesis. The electroencephalogram showed

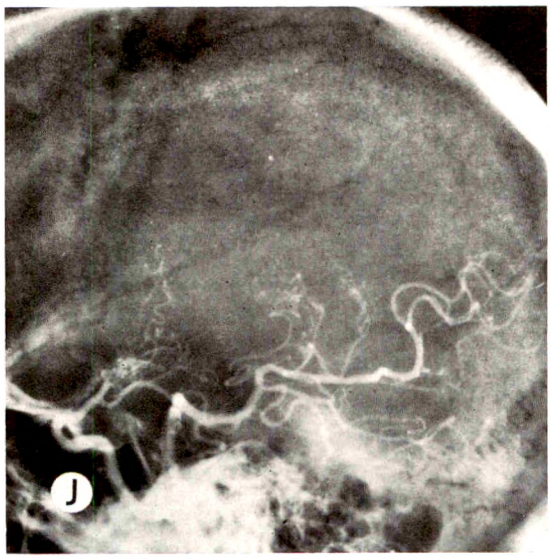


FIG. 2. (*J*) Right brachial angiography on August 8, 1966, shows a normal filling of the basilar artery. The right internal carotid artery is narrow and is obstructed at its bifurcation; its appearance has not changed from the previous examination. However, there is considerable change in the appearance of the right posterior cerebral artery (the frontal angiogram showed that the one outlined here is the right side) which in the original right sided carotid angiogram (*G*) showed marked narrowing in its proximal 2 cm. It would be difficult to attribute the change in the left carotid system and in the right posterior cerebral artery merely to spasm. I would consider it as possibly due to reversal of the pathologic process.

only diffuse slowing with minor right posterior slow focal trend.

The hemiparesis improved somewhat and she was discharged. Within 3 or 4 weeks, the patient was walking and riding her bicycle. They thought that the child was somewhat slower than her older brother, but otherwise was doing well. However, she again had sudden episodes of blank stare and loss of speech momentarily. Sometime later she developed dragging of her left foot more than usual, as well as staggering. For that reason, she was brought back to Washington University Medical Center where she was readmitted and angiography was repeated. The neurologic examination at the time of the second admission revealed an old left hemiparesis and was otherwise unremarkable. A follow-up in 1968 (age 7 years) at which time she was admitted to Bowman Gray Medical Center in Winston Salem, North Carolina, showed that the child was developing well physically. The weakness of her left extremities was severe, her I.Q. was estimated at 70. Repeat bilateral angiography (right brachial and left carotid) showed no change in the angiographic findings from the examination performed 4 years earlier.

Roentgenologic examination. The skull was normal.

Bilateral carotid (Fig. 3, *A–C*; and 3, *D–F*) and right brachial (Fig. 3, *G–J*) angiography performed on October 21, 1963, and June 18, 1964, showed bilateral occlusion of the internal carotid arteries in the supraclinoid portion. The basilar artery was normal. There was an extraordinary vascular network in the region of the basal ganglia arising from the basilar artery system as well as from the supraclinoid portion of the internal carotid arteries which resulted in eventual filling of all of the major arteries in the middle and anterior cerebral artery territories. In addition, there was evidence of collateral circulation by transdural external-internal carotid anastomoses (*rete mirabile*). The transdural anastomotic network arising from the meningeal branches of the ophthalmic artery was particularly noteworthy.

Case IV. M.N. is a 42 year old Japanese woman who was admitted to the Quakini Hospital in Honolulu because the prior week while driving her car she developed left hemiparesis. The history showed that some 7 months before she had developed a 15 minute episode of left sided weakness. At that time she had some studies

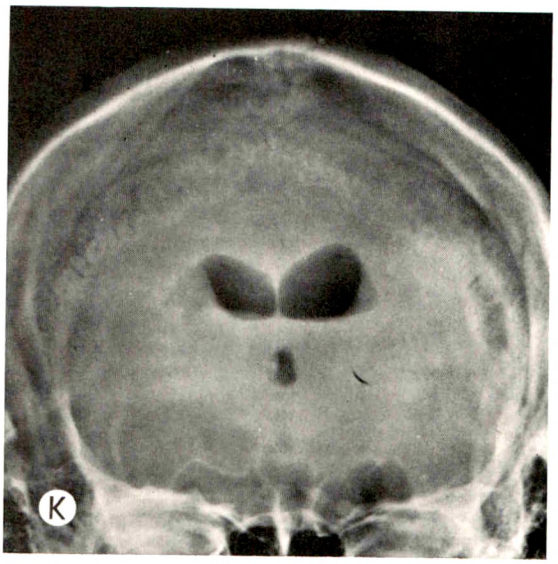


Fig. 2. (*K*) A pneumoencephalogram made in 1968 shows mild ventricular dilatation more marked on the left side.

performed in Los Angeles, California, including cerebral angiography. In the interim, the patient never returned to work following this original episode and was said to have an emotional disorder. She was placed under psychiatric care and was receiving thorazine. Some 3 weeks before admission she complained intermittently of dragging her left foot and of left sided weakness. This had progressively become worse so that at the time of admission she had an obvious left hemiparesis. She also complained of difficulty of opening her mouth and swallowing, and had some difficulty with her speech. Upon admission, the patient was mute. She seemed very fearful and did not utter any words. She seemed to understand spoken language and would obey some commands. There appeared to be a left homonimous hemianopsia.

Neurologic examination. This showed a spastic left hemiparesis greater in the left arm. All reflexes were hyperactive, more on the left. Physical examination was normal aside from a pelvic mass.

Clinical course. She was in the hospital for some 4 months and was finally discharged to go home. In the meantime, she has gotten progressively worse. She whimpered both when she was pleased and when she was unhappy. She mumbled short phrases to express herself. She was able to feed herself and walked about without aid. An abdominal exploration had discovered an ovarian carcinoma with peritoneal seeding

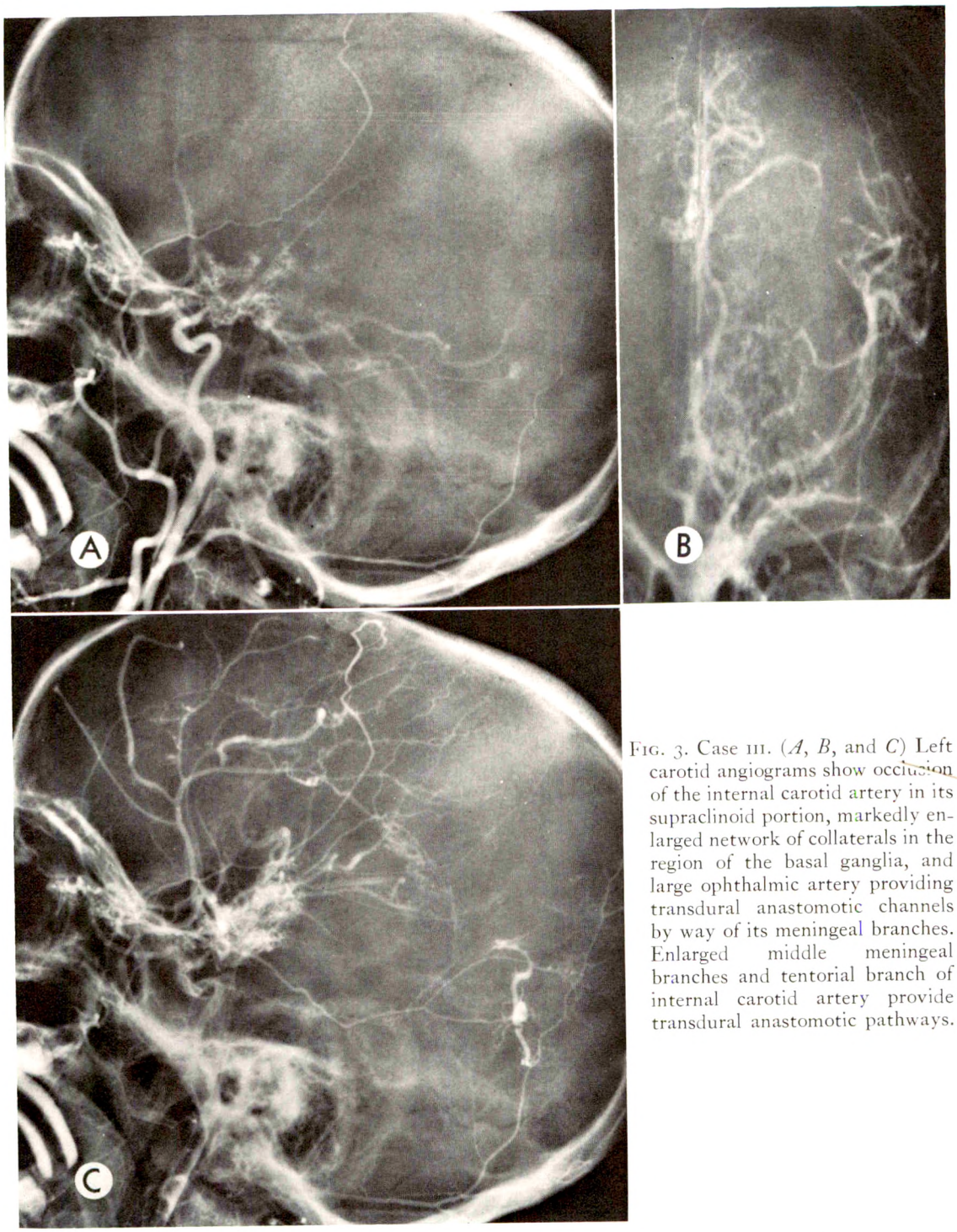


FIG. 3. Case III. (*A*, *B*, and *C*) Left carotid angiograms show occlusion of the internal carotid artery in its supraclinoid portion, markedly enlarged network of collaterals in the region of the basal ganglia, and large ophthalmic artery providing transdural anastomotic channels by way of its meningeal branches. Enlarged middle meningeal branches and tentorial branch of internal carotid artery provide transdural anastomotic pathways.

and liver involvement. Radiation therapy was given. At the time of discharge, the patient's mentality had continued to deteriorate. The patient died in Hawaii 2 years and 2 months after the initial episode of hemiparesis.

Autopsy. The body was that of an emaciated woman. There was metastatic solid papillary ovarian adenocarcinoma involving the sigmoid colon and the terminal ileum (with perforations), the bladder and the pelvic wall. There

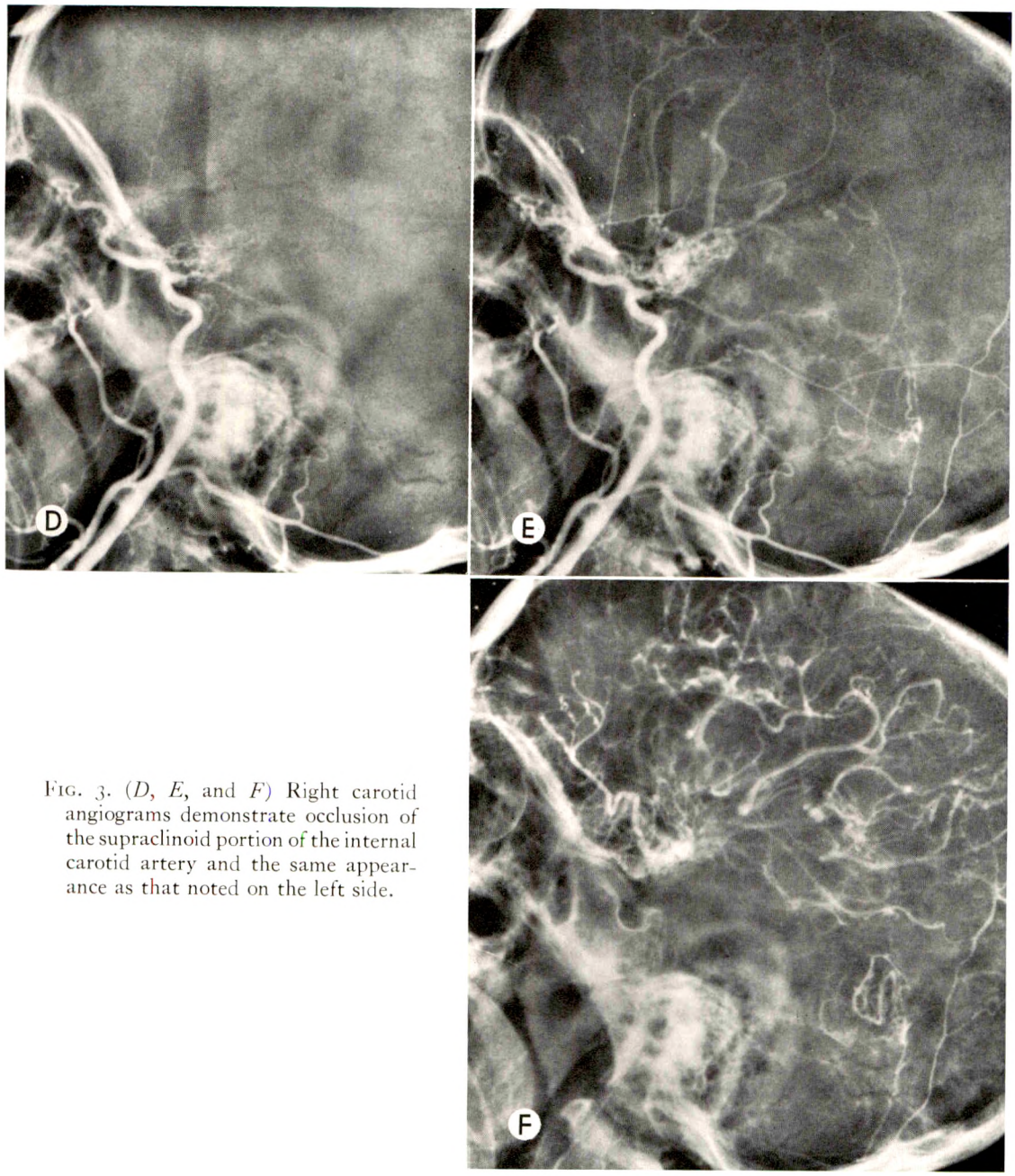


Fig. 3. (*D*, *E*, and *F*) Right carotid angiograms demonstrate occlusion of the supraclinoid portion of the internal carotid artery and the same appearance as that noted on the left side.

was a bilateral acute pyelonephritis. The brain showed evidence of old cerebral infarcts of the left and right frontal lobes, right frontal parietal region and basal ganglia. There was evidence of cerebral atrophy. The circle of Willis was described as appearing intact but involved with a mild amount of "arteriosclerotic discoloration." Unfortunately, no attempt was made to study the vessels carefully.

Roentgenologic examination. Left carotid angiography on June 8, 1964 revealed the presence of localized narrowing at the bifurcation of the intracranial internal carotid artery involving the 3 vessels, internal carotid, anterior, and middle cerebral arteries (Fig. 4, *A* and *B*). Right carotid angiography was not performed (technical difficulties?).

Bilateral carotid angiography performed on January 13, 1965 (Fig. 4, *C–E*; and 4, *F* and *G*) demonstrated occlusion of both internal carotid

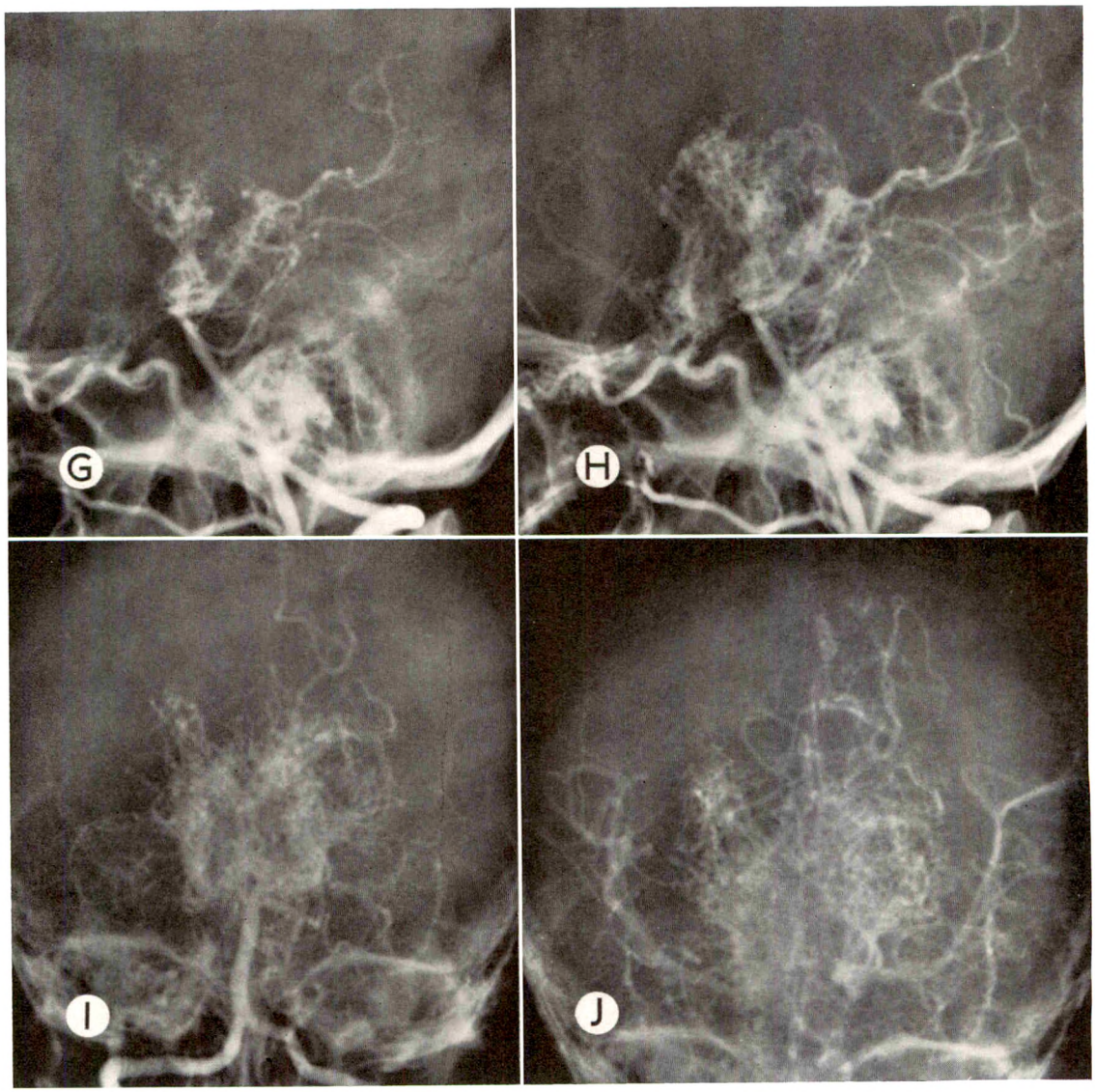


FIG. 3. (*G*, *H*, *I*, and *J*) Right brachial angiograms demonstrate spectacular spongy network of vessels in the basal ganglia bilaterally and eventual filling of middle cerebral and anterior cerebral artery branches.

arteries in the supraclinoid portion just at the place where the artery would normally bifurcate. Filling of the anterior and middle cerebral arteries took place by way of collateral connections with the branches of the posterior cerebral artery and by way of deep perforating branches. Filling of both anterior cerebral arteries was somewhat incomplete showing no filling of the proximal 2 to 3 cm. of the pericallosal artery. The development of the deep collateral channels in the basal ganglia region was very minor in this case and there was no evidence at the time of this angiography of development of transdural external-internal carotid anastomoses (*rete mirabile*).

In summary, this was a 42 year old Japanese woman who developed intermittent left hemiparesis accompanied by some mental symptoms which were thought to be psychiatric in nature. The neurologic and mental symptoms became progressive and the patient deteriorated over a period of a year to the point where she was unable to function properly. A carcinoma of the ovary was discovered which may have been the direct cause of death. Angiography showed originally only narrowing at the bifurcation of

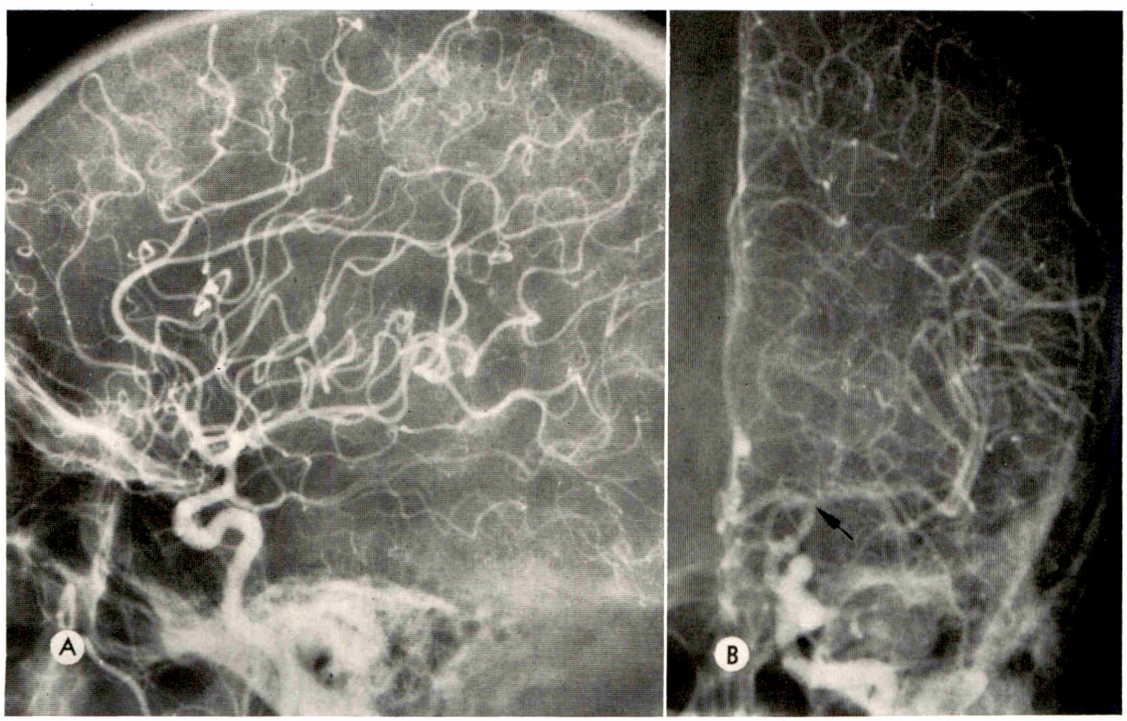
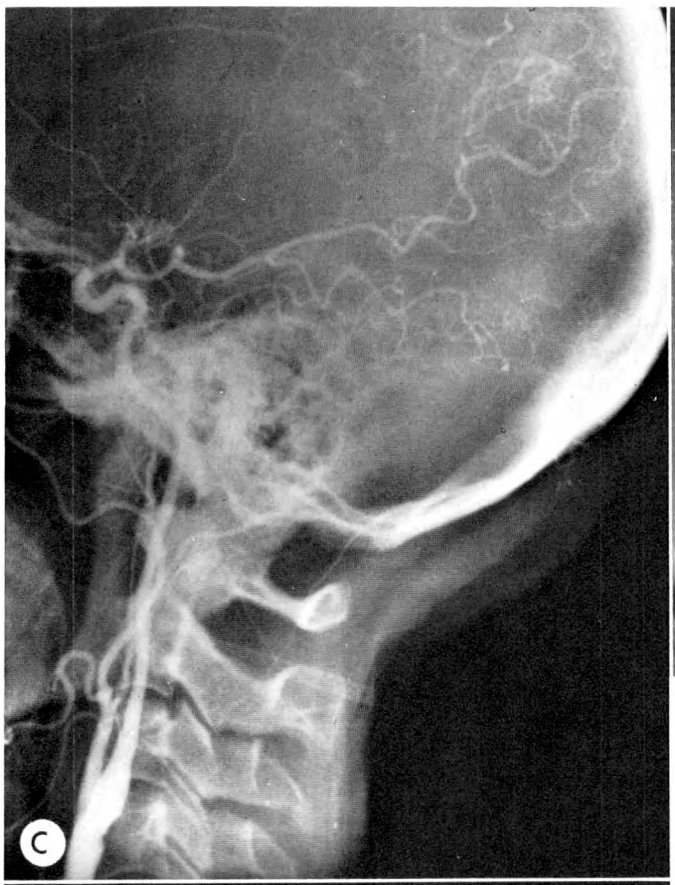


Fig. 4. Case iv. (*A* and *B*) Left carotid angiography performed on June 8, 1964, shows narrowing of the supraclinoid portion of the internal carotid artery with marked narrowing at the exact point of bifurcation of the internal carotid artery involving the distal internal carotid artery, the middle and the anterior cerebral arteries (arrow in *B*).

the internal carotid artery and repeat angiography 7 months later showed bilateral supraclinoid internal carotid occlusions.

Case v. A.C. is a 4 year old girl who had onset of *right* hemiparesis and aphasia. At that time, she also had some tonic-clonic movements of the right leg. Four months later, she developed *left* sided hemiparesis; twitching of the left extremities was also noted. She was admitted to the University Hospital in Gainesville, Florida, at which time physical examination showed bilateral hemiparesis more evident on the right than the left, and a right sided hemianopsia. Routine laboratory studies were normal. The sedimentation rate was 30 mm. per hour and LE preparations were negative. Sickle cell studies were negative. The cerebrospinal fluid was normal. EEG showed paroxysmal dysrhythmia with dominance of the right cerebral hemisphere. The child had 1 or 2 more episodes of loss of speech and worsening of the bilateral hemiplegia until the last one at which time she was unable to speak for some time. In the succeeding 13 months she remained essentially aphasic, although she was able to communicate with her parents to let them know when she was hungry. When last seen, 2 years after the initial admission and $2\frac{1}{2}$ years after the original episode, she was mentally retarded, almost completely aphasic, and had bilateral hemiplegia. The only thing she could do was crawl around but was unable to stand or walk.

Roentgenologic examination. The skull was essentially normal. Bilateral carotid angiography performed at the time of the initial admission showed that the left carotid artery was almost completely occluded at its bifurcation. Partial filling of the anterior and the middle cerebral arteries was obtained but whether this was by direct connection through irregular, possibly recanalized, channels or by way of anastomotic pathways could not be stated. There were many dilated perforating branches. The right carotid angiogram revealed a localized area of narrowing in the supraclinoid portion of the carotid syphon which was situated slightly below the bifurcation of the intracranial internal carotid artery. At the time that the angiography was performed, this was the only de-





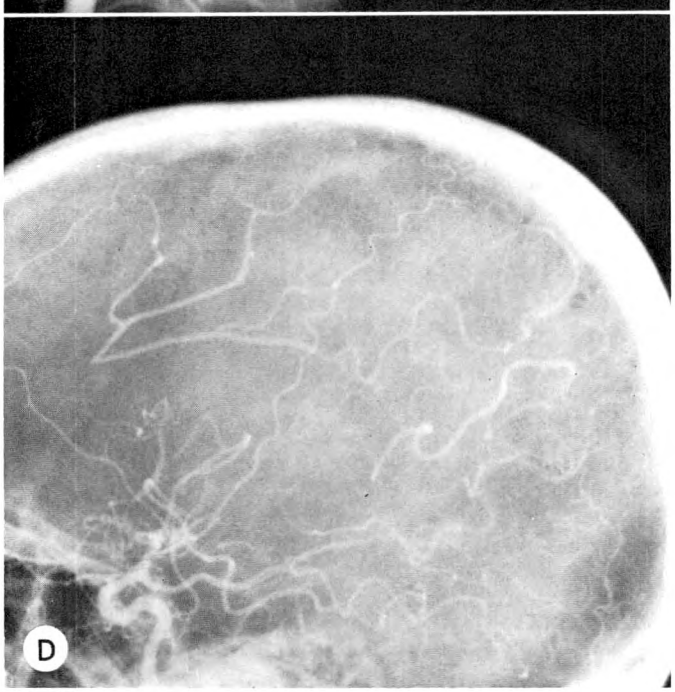


FIG. 4. (*C*, *D*, and *E*) Left carotid angiography performed on January 13, 1965, shows occlusion of the internal carotid artery in the supraclinoid portion and a relatively scanty development of the dilated fine collaterals in the region of the basal ganglia. The anterior cerebral artery is evidently completely occluded and its distal portion fills by way of collateral channels, but the proximal portion never filled in the serialogram. The internal carotid artery is much narrower than previously and the narrowing starts 1 or 2 cm. above the common carotid bifurcation.

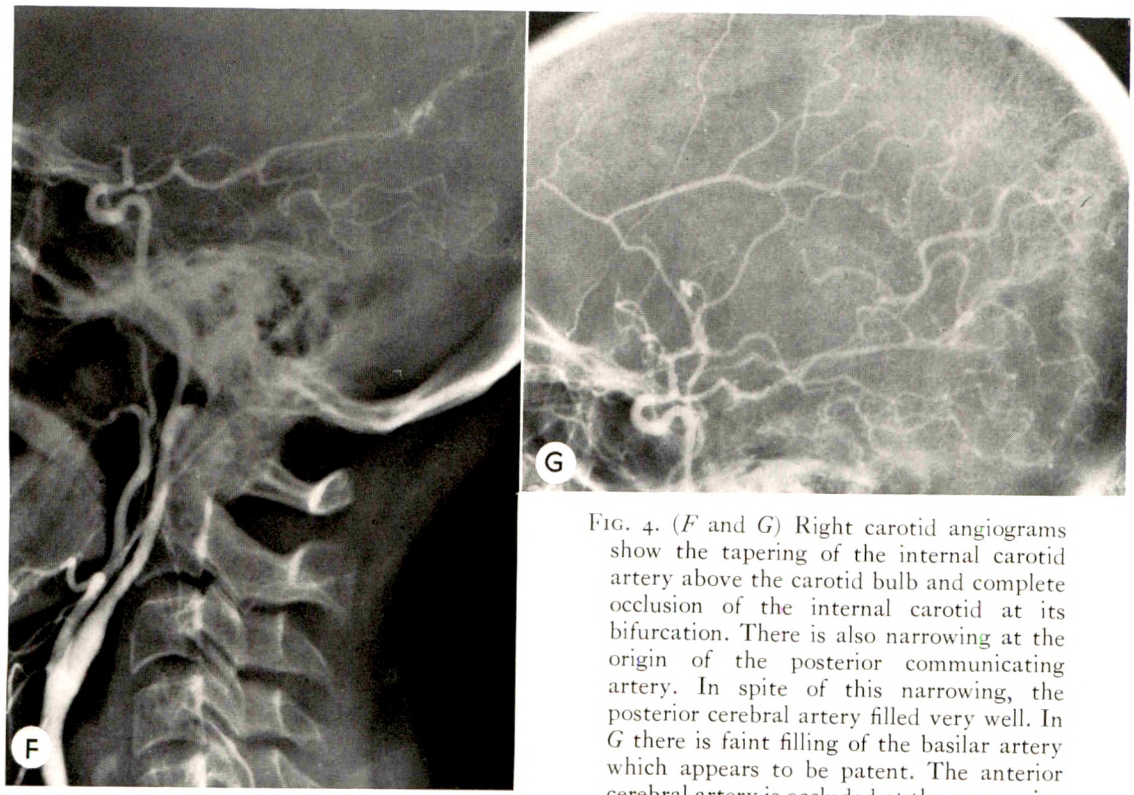


Fig. 4. (*F* and *G*) Right carotid angiograms show the tapering of the internal carotid artery above the carotid bulb and complete occlusion of the internal carotid at its bifurcation. There is also narrowing at the origin of the posterior communicating artery. In spite of this narrowing, the posterior cerebral artery filled very well. In *G* there is faint filling of the basilar artery which appears to be patent. The anterior cerebral artery is occluded at the same point as on the left side so that the entire proximal 3 to 5 cm. appears to be occluded.

monstrable lesion on this side. However, historically other episodes occurred later involving particularly the left extremities. The angiography was not repeated, however.

In summary, this is a child who between the age of 3 and 4 years began to develop neurologic symptoms consisting of hemiplegia on the right side and some 4 to 5 months later, hemiplegia on the left side, accompanied by other neurologic manifestations. She improved after both attacks but had other attacks within the succeeding 13 months which left her almost completely paralyzed and aphasic as well as retarded, but the degree of mental retardation cannot be evaluated because of the aphasia. Bilateral carotid angiography showed occlusion of the internal carotid artery at the origin of the anterior and middle cerebral arteries with collateral circulation through the basal ganglia. The right side showed only stenosis of the supraclinoid portion of the internal carotid artery.

Case vi. A.K. is a $7\frac{1}{2}$ year old girl whose chief complaint was recurrent intractable headaches with throbbing for the last 4 years associated with nausea, vomiting, and abdominal pain which were incapacitating. She had a giant hemangioma on the right side of the face noted shortly after birth which involved the right eye, right side of the palate and the lower lip. She was being treated by a plastic surgeon and also received radiation therapy with radon seeds.

Neurologic examination. This was essentially normal aside from a cataract in the right eye and questionable decreased pin prick sensation in the right lower extremity. The reflexes were bilaterally normal and equal. She had above normal intelligence. It was felt that she had been right-handed during the first 1 to 2 years of life and after that seemed to be exclusively left-handed.

Laboratory examinations. These were normal.

Roentgenologic examination. Bilateral carotid and bilateral brachial angiographies were carried out which demonstrated occlusion of both internal carotid arteries and of the basilar artery with filling of the intracranial branches by way of transdural external-internal carotid anastomoses seen everywhere, near the base of the skull, over the vault, in the region of the ten-



FIG. 5. (*C*) Right brachial angiography shows non-visualization of the right internal carotid artery and a large anastomotic network at the base of the skull from the external carotid branches. There is enlargement of the middle meningeal artery and its branches as well as the occipital artery (upper arrow) and branches thereof. The right vertebral artery is shown (2 arrows) and does not go beyond the base of the skull. Left brachial angiography was also performed which revealed filling of the vertebral artery only up to the base. The basilar artery was occluded and all of the circulation of the posterior fossa as well as of the supratentorial region took place by way of external-internal carotid anastomoses (*rete mirabile*) and on the left side also by means of network collaterals in the base of the brain.

torium, and around the falx (Fig. 5, *A* and *B*; and 5*C*). The right internal carotid artery could not be seen on the angiogram and the question of congenital absence of this artery was raised. Tomograms of the petrous pyramid revealed a carotid canal on the left side but on the right side no carotid canal could be demonstrated.

This case will be reported in detail separately because of some rather unusual features.[37]

In summary, this is a $7\frac{1}{2}$ year old child who was essentially neurologically negative and had only intractable recurrent incapacitating throbbing headaches. She was of normal intelligence and the only feature which may be indicative of neurologic deficit was the fact that between 1 and 2 years of age she seemed to have changed handedness. It is interesting that in her case, practically all of the blood supply is coming by way of transdural external-internal carotid anas-

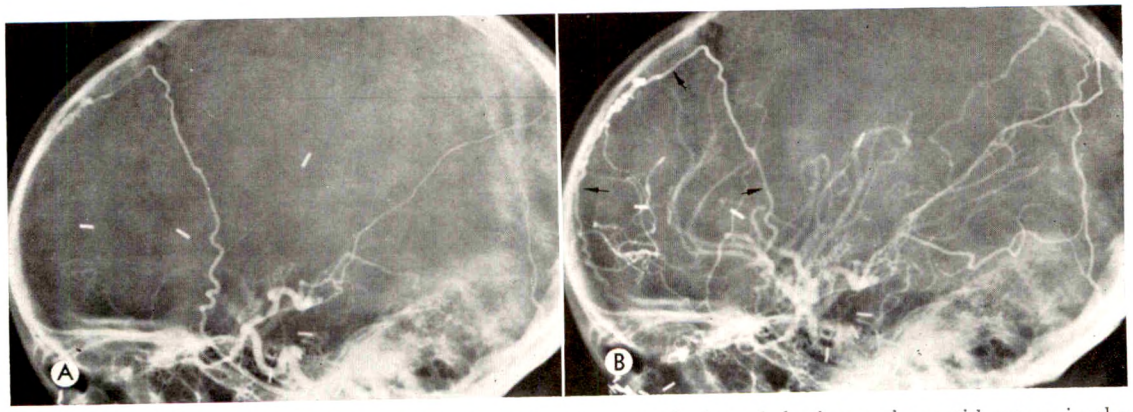


FIG. 5. Case VI. (*A* and *B*) Left carotid angiography shows occlusion of the internal carotid artery in the supraclinoid portion. The posterior communicating artery is large and shows marked narrowing at its origin. A fine network of collaterals is seen in the base of the brain with eventual filling of the middle and anterior cerebral branches. This filling is taking place partly by way of transdural external-internal carotid anastomoses arising from the ophthalmic artery as well as from branches of the middle meningeal artery (arrows).

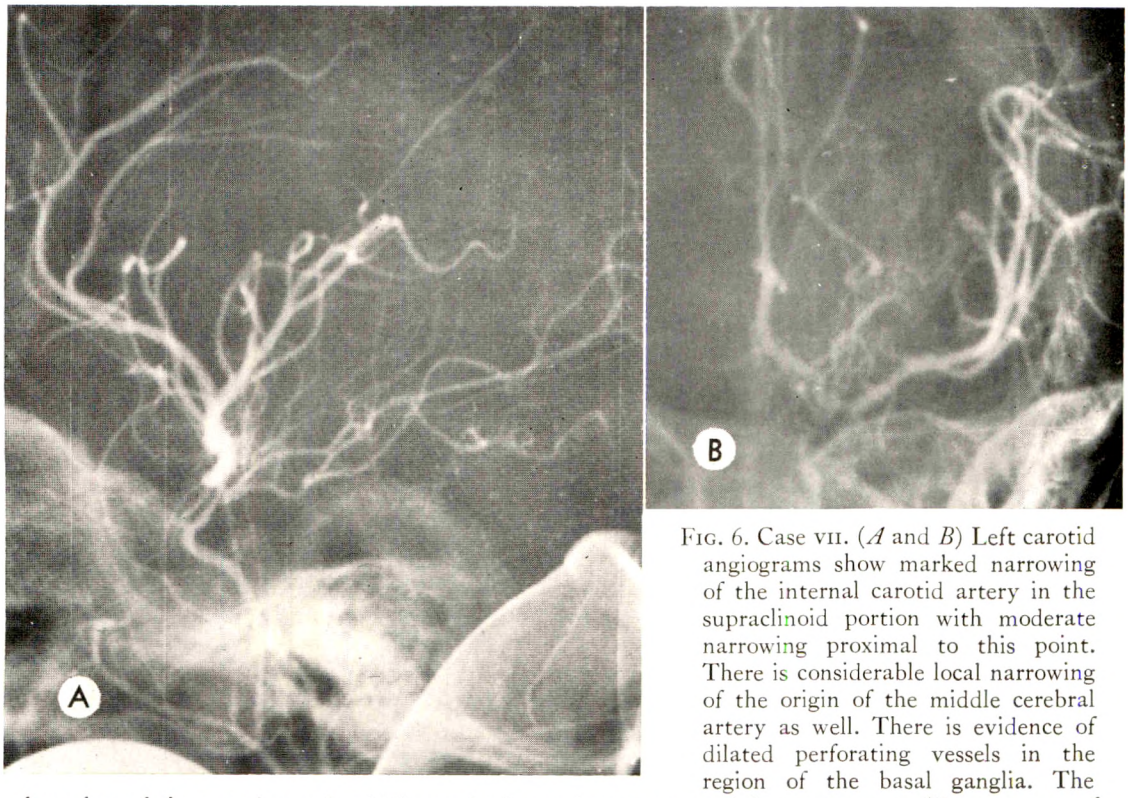


Fig. 6. Case VII. (*A* and *B*) Left carotid angiograms show marked narrowing of the internal carotid artery in the supraclinoid portion with moderate narrowing proximal to this point. There is considerable local narrowing of the origin of the middle cerebral artery as well. There is evidence of dilated perforating vessels in the region of the basal ganglia. The branches of the anterior and middle cerebral arteries are normal in appearance. (By courtesy of Williams and Wilkins, and *Clinical Neurosurgery*, 1961.)

tomoses (*rete mirabile*) and there is only moderate development of the enlarged perforating branches in the basal ganglia region which is such a prominent feature in the majority of these cases.

Case VII. P.L. is a 7 month old girl from Haiti who was brought to the Neurological Institute of New York with a chief complaint of paralysis of the right arm and leg. At the age of 4 months, she had an upper respiratory infection. The weight gain was poor, gaining only 1 pound between the ages of 5 and 7 months. Ten days prior to admission, she was irritable and cried during the entire night. The following day "puffiness of the face" and distant stare were noted. Her head was turned to the left. There was no fever. A spinal tap was done which was bloody. Some days later, repeat spinal puncture showed a clear fluid. She had another febrile episode a few days later.

On admission, her temperature was 99° F. and she had a right hemiplegia. Bilateral carotid angiography was carried out. Approximately 7 days after the angiography, she developed weakness of the left extremities and had a bilateral hemiplegia. This was not attributed to the angiography inasmuch as it developed several days after the procedure.

She improved very little in the ensuing months and finally died 10 months later in Haiti. There was no autopsy.

Roentgenologic examination. Angiography revealed a partial occlusion of both internal carotid arteries at the bifurcation of this artery intracranially. Below this point there was considerable narrowing of the internal carotid artery extending down to its origin, which was suggestive of a diffuse process. There was a question of a small saccular aneurysm in the trunk of the middle cerebral artery. Considerable dilatation of the perforating branches in the region of the basal ganglia was noted bilaterally (Fig. 6, *A* and *B*; and 6, *C* and *D*).

In summary, this is a 7 month old child who developed hemiplegia first on one side, then on the other, preceded by a poorly defined febrile illness, and who demonstrated angiographically

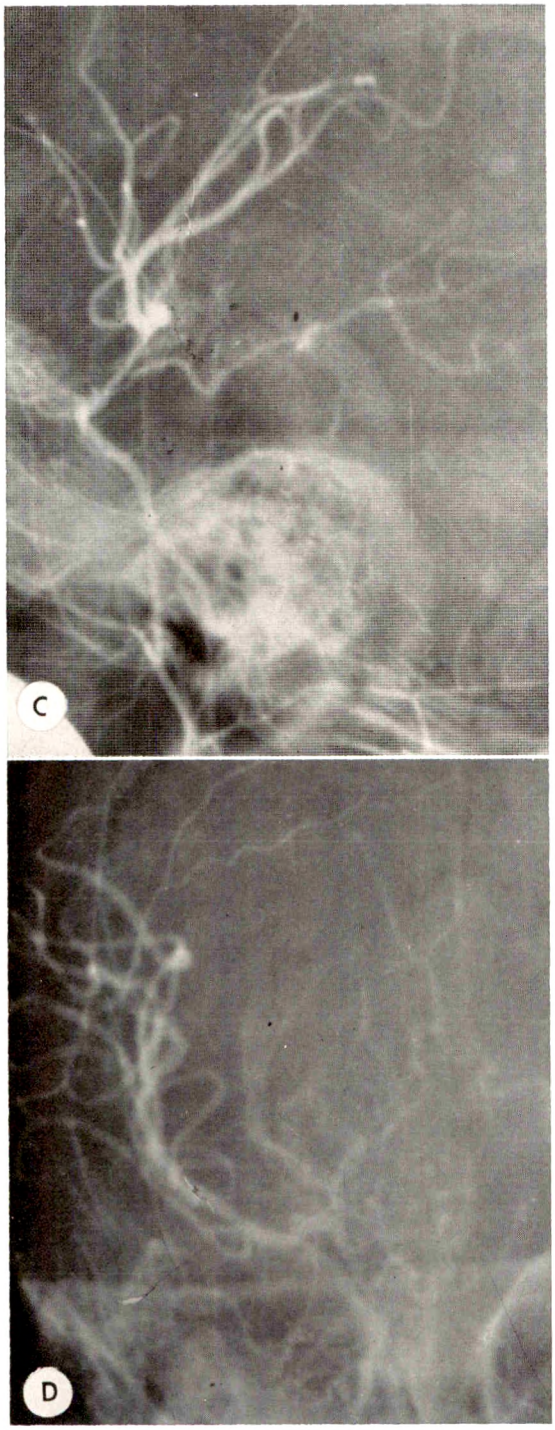


FIG. 6. (*C* and *D*) Right carotid angiograms show an identical appearance to that noted on the left side. There appears to be a small aneurysm in the region of the trunk of the middle cerebral artery.

almost complete occlusion of the internal carotid artery on both sides at the intracranial bifurcation of this vessel with considerable increase in the vascularity in the region of the basal ganglia. The child died 10 months later at the age of 15 months.

Comment. I believe that this case illustrates the angiographic picture in the initial stages of the development of the disease process under discussion in this paper.

CASE VIII. P.M., a 41 year old man, was admitted to Barnes Hospital of St. Louis complaining of transient episodes of loss of vision of both eyes for 1 to 2 minutes, especially when he got up and walked or when he was upset or excited. He had previously been in good health, except for an irritable mood, until 3 years prior to admission when he had an episode of twitching in his right eye lasting for a few minutes. At this time he saw a doctor who found slightly elevated blood pressure, and placed him on medicine. He has occasionally complained of dizziness, feeling himself spinning without nausea or vomiting or unsteady gait. One year prior to admission he noted numbness and slight weakness in his left arm which lasted for 1 week. For the past month he has had episodes of loss of vision. He had had frontal headaches once in awhile. His memory has been gradually poor for the last 2 years. Neurologic examination showed a left homonomous hemianopsia and was otherwise negative. Blood pressure was 150/80. Laboratory tests were negative; a lumbar puncture revealed clear fluid at normal pressure, and normal protein. An electroencephalogram was indeterminate.

Right brachial angiography (Fig. 7, *A–D*) was carried out and this was followed by ventriculography (Fig. 7, *H* and *I*). He was well after the ventriculography but several hours later complained of excessive heat in the room and vomited. Blood pressure was measured and was 220/110 Hg and the pulse was 64. He became aphasic and developed a right hemiplegia. About an hour later he was completely comatose and decerebrate. Emergency left angiography (Fig. 7*F*) and additional roentgenograms with the residual air from the preceding ventriculography (Fig. 7*G*) demonstrated a left sided mass which turned out to be a large subdural hematoma that was evacuated. The patient did not respond well and has remained in a poor neurologic state for many months.

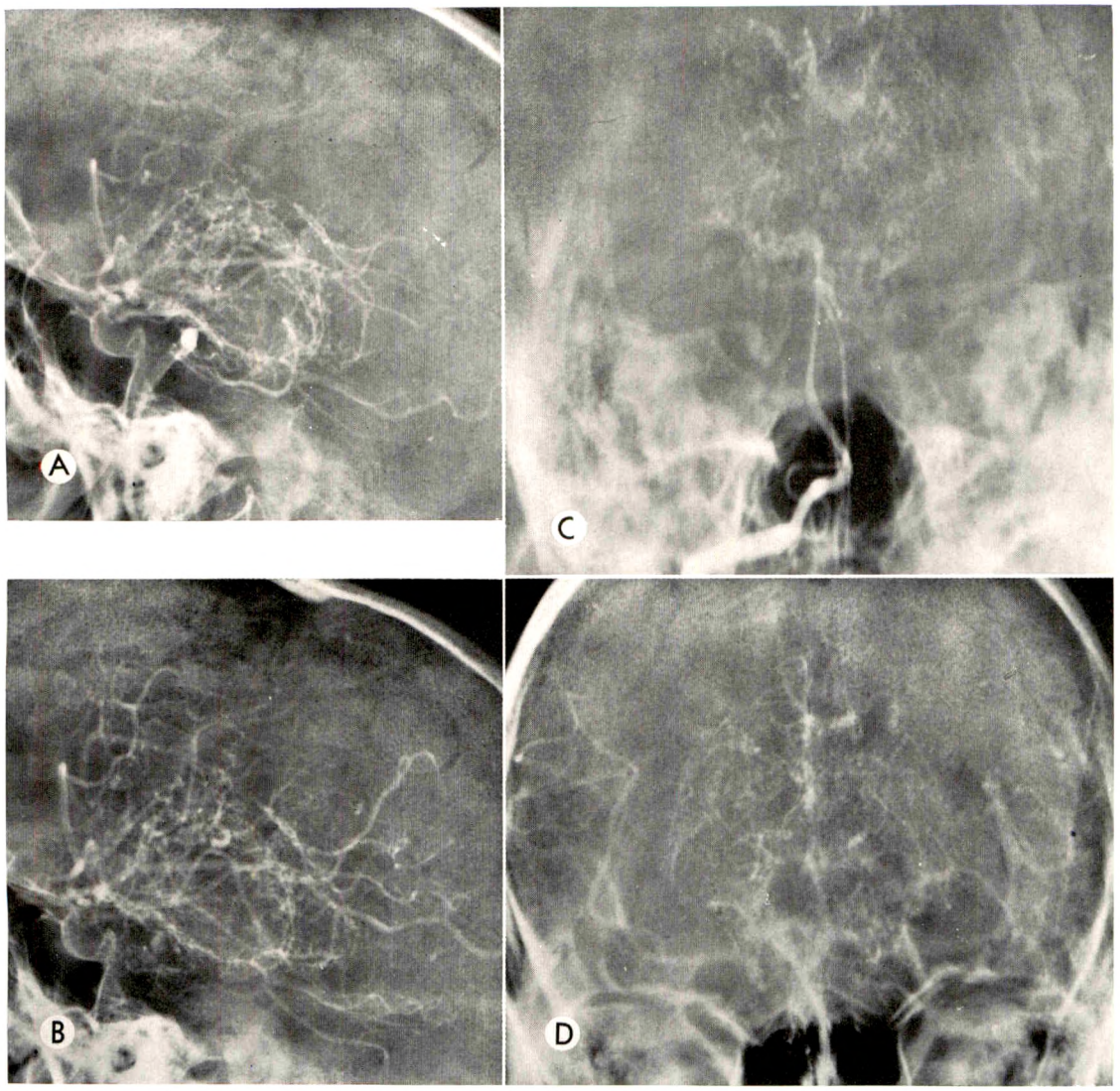


Fig. 7. Case VIII. (*A*, *B*, *C*, and *D*) Right brachial angiograms show good filling of the basilar artery, which is slightly narrow. A large network of fine collateral vessels is seen bilaterally in the region of the basal ganglia, and eventually most branches of the middle cerebral and anterior cerebral arteries fill. The right internal carotid artery was occluded just above the origin of the ophthalmic artery and was well filled in the later phases of the angiogram.

Roentgenologic examination. The skull was negative. Right brachial angiography demonstrated complete occlusion of the right internal carotid artery just above the origin of the ophthalmic artery (Fig. 7, *A–D*). The artery suddenly becomes narrow about 2 cm. above the bifurcation of the common carotid artery and remains narrowed to the point of occlusion. Many thin arterial branches are seen to arise and proceed to the cranial cavity from the region of the obstruction, probably from branches normally supplying the meninges in the region of the cavernous sinus via transdural external-internal carotid anastomoses (*rete mirabile*). Transdural anastomoses are also seen arising from the ophthalmic artery (Fig. 7, *J* and *K*). The basilar artery is narrow and gives rise to a large network of fine vessels in the region of the thalamus bilaterally. This network eventually produces bilateral filling of the branches of the middle cerebral artery. The left carotid artery is almost completely occluded approximately 2 cm. above the bifurcation of the common carotid artery, but a very

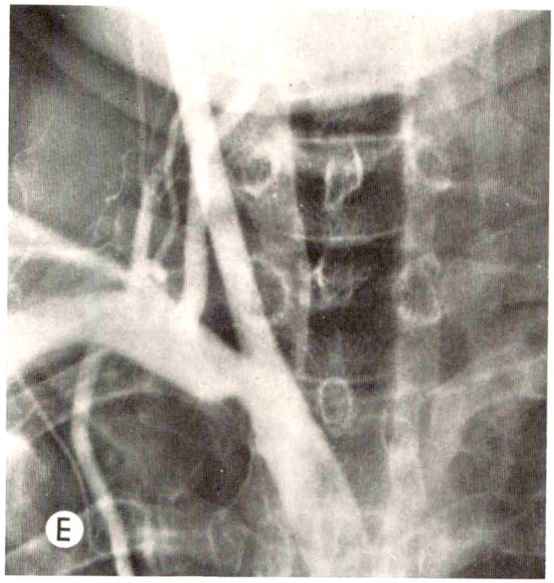


FIG. 7. (*E*) Right brachial angiogram shows good filling of the right vertebral artery. An atherosclerotic plaque is seen in the subclavian artery.

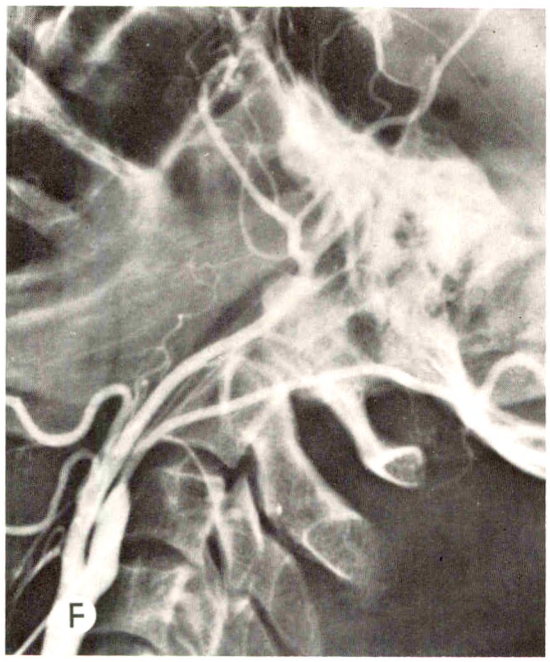


FIG. 7. (*F*) A left carotid angiogram obtained after ventriculography demonstrates high occlusion of the internal carotid artery. Considerable narrowing or almost complete occlusion of the cervical portion of this artery is seen starting about 2 cm. above the bifurcation of the common carotid artery.

thin line of contrast can be seen to ascend towards the base of the skull and a similar filling of a network of fine vessels just above the usual site of entrance of the internal carotid artery into the skull is seen as well as filling of the pericallosal artery. There is also evidence of transdural external-internal carotid anastomotic filling in the posterior parietal region from both carotid arteries.

An additional feature in this case is that the right internal carotid artery below the syphon showed, in addition to the narrowing, moderate irregularity suggesting atherosclerosis. The right brachial angiogram demonstrated an atherosclerotic plaque in the subclavian artery (Fig. 7*E*).

In summary, this is a 41 year old man who for several years had complained of an irritable mood and several episodes indicating neurologic involvement, including one episode of weakness of the left arm lasting for a week. The last episode involved transient loss of vision and finally left hemianopsia. Angiography revealed multiple vascular occlusions with a vascular network in the basal ganglia. Ventriculography showed a normal ventricular system. There was considerable subdural air. Possibly, one of the transdural anastomotic vessels ruptured and a subdural hematoma developed

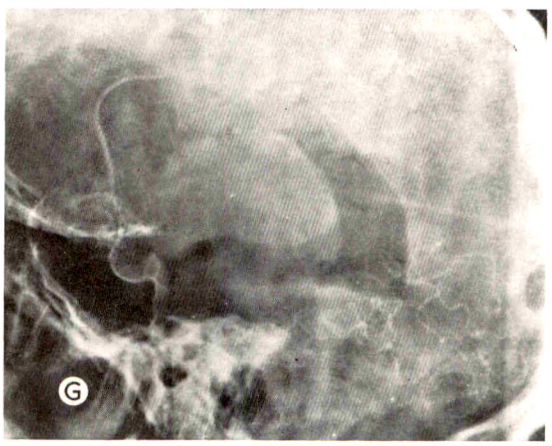


FIG. 7. (*G*) Tail-end of a repeat left carotid angiogram obtained after ventriculography, when the patient became ill, demonstrates the presence of dilated thin collaterals in the suprasellar region which resulted in filling of the pericallosal artery. There is also noted filling of intracranial branches in the occipital region which were felt to be taking place by way of transdural external-internal carotid anastomoses.

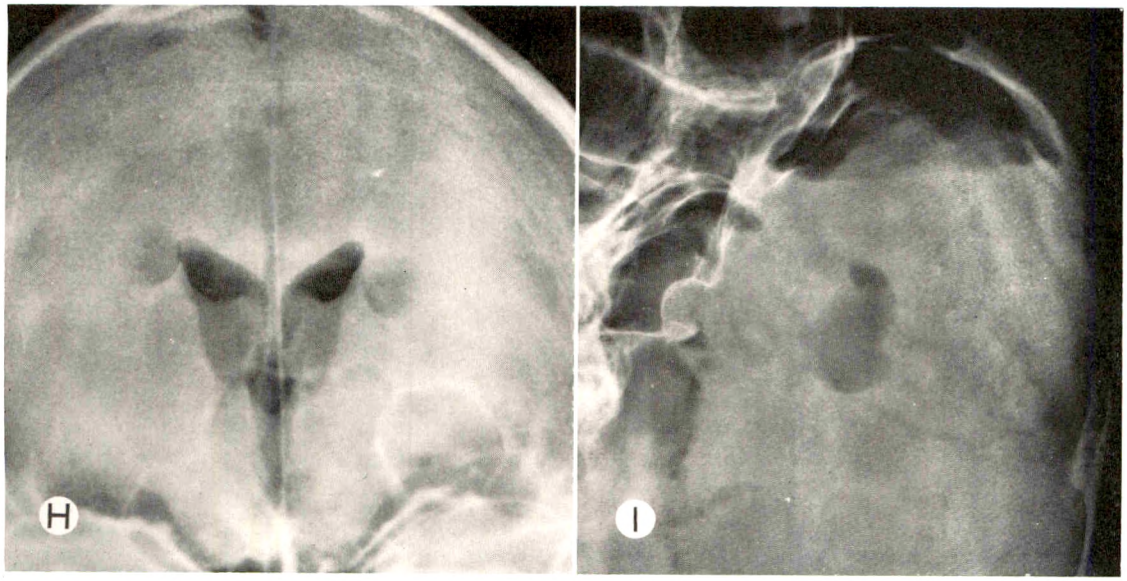


Fig. 7. (*H* and *I*) Frontal and lateral views taken during ventriculography demonstrate undisplaced and normal appearing lateral ventricles and a fairly large collection of subdural air.

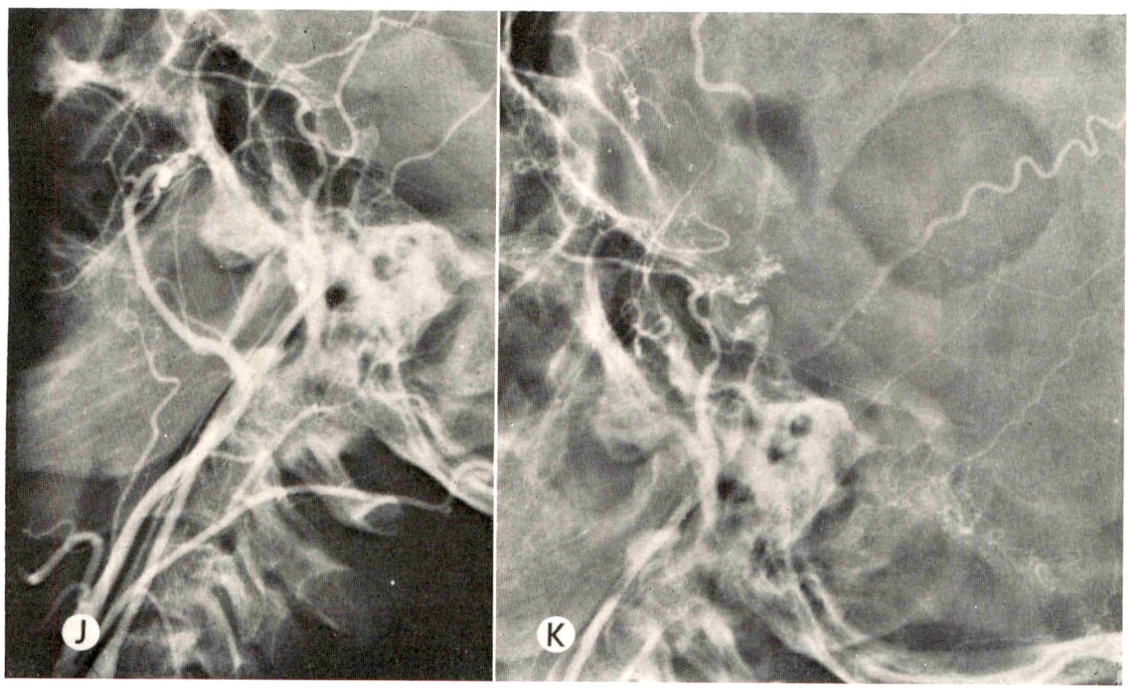


Fig. 7. (*J* and *K*) Repeat right carotid angiography by direct puncture performed after evacuation of the subdural hematoma, which developed several hours after ventriculography. It demonstrates to better advantage the occlusion of the internal carotid artery just above the origin of the ophthalmic artery with the development of fine collaterals probably arising from the cavernous sinus branches of the internal carotid artery. There is slight irregularity in the artery at one point in the intracavernous portion of the vessel suggesting an atherosclerotic plaque. Considerable narrowing of the internal carotid artery above the carotid bulb is present.

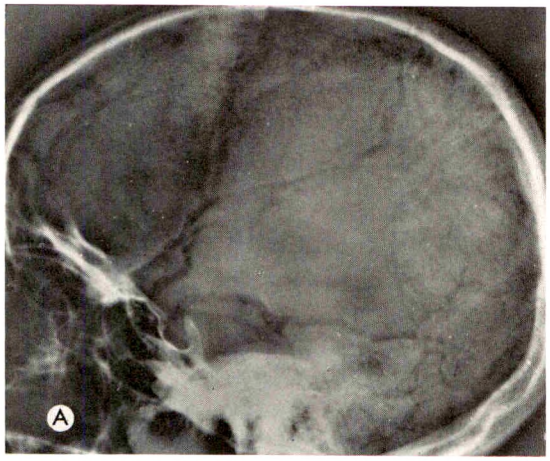


Fig. 8. Case ix. (*A*) Lateral roentgenogram of the skull demonstrates enlargement of the middle meningeal channels on both sides.

within 4 to 6 hours which rapidly led to coma and decerebrate rigidity.

Case ix. I.M., a 16 year old Negro girl, was admitted to the Jewish Hospital of Brooklyn. For the last 4 months she had had episodes of falling without loss of consciousness. There was a question as to whether she may have been having convulsions. On neurologic examination, she had numbness of the right side of her body, reduction in sensation and loss of power in the right upper extremity. A diastolic murmur in the aortic region was heard and felt to be due to aortic insufficiency. Serologic tests for syphilis were negative. There was a history suggestive of rheumatic fever. Right brachial and left carotid angiography was performed. A follow-up 1 year later indicated that the patient's falling spells had improved. In the meantime, she had been placed on dilantin and phenobarbital medication.

Roentgenologic examination. The plain roentgenograms of the skull demonstrated increase in the size of the middle meningeal grooves (Fig. 8*A*). Left carotid angiography (Fig. 8, *B–E*) demonstrated occlusion of the internal carotid artery just above the ophthalmic artery. A fine network of vessels was seen just above the occluded internal carotid artery, evidently in the basal ganglia region. The middle meningeal artery arose directly from the ophthalmic artery (this is not a rare anomaly) and was seen to ascend up to the region of the superior sagittal sinus in the bregmatic region. The anterior meningeal artery also filled and eventually a fine network of vessels in the region of the corpus callosum was visualized. The ophthalmic artery also contributed to the filling of the inferior frontal region via the same external-internal carotid anastomotic pathways (*rete mirabile*). It is also noted that the tentorial branch of the internal carotid artery arising from the intracavernous portion of the carotid syphon (artery of Bernasconi and Casinari) also filled and eventually produced some filling in the posterior temporal region. Right brachial angiography (Fig. 8, *F* and *G*) demonstrated occlusion of the right internal carotid artery just above the level of the ophthalmic artery. The basilar artery filled and a large network of fine vessels filled in the region of the basal ganglia bilaterally by way of branches of the basilar artery and from the stump of the occluded carotid artery. The middle meningeal artery on this side arose from its normal site and was also enlarged, leading to some filling of intracranial branches via the same external-internal carotid anastomoses.

Case x. C.K. was a 42 year old man who was admitted to the Pittsburgh Veterans Administration Hospital with a history of sudden subarachnoid hemorrhage occurring 3 months prior to admission. He was in another hospital in a comatose state for 5 weeks and slowly recovered from this. It was impossible to determine whether the original episode had been preceded by headache. At the time of admission to the hospital, he was intact neurologically. The angiographies were performed as part of his diagnostic work-up.

Roentgenologic examination. Angiography (Fig. 9, *A* and *B*) revealed bilateral occlusion of the internal carotid artery in the supraclinoid portion with considerable increase in the size of perforating branches. The network of vessels at the base of the brain was less pronounced than is usually the case in children, but the appearance was quite similar. The basilar artery was not visualized. There was a prominent collateral flow by way of anterior and posterior choroidal arteries.

In summary, this patient presented with a subarachnoid hemorrhage and after a stormy course, where he was comatose for a period of 5 weeks, recovered completely and had essentially a normal neurologic examination.

Analysis of Roentgenologic Changes

The plain roentgenograms are negative unless the circulation by way of transdural

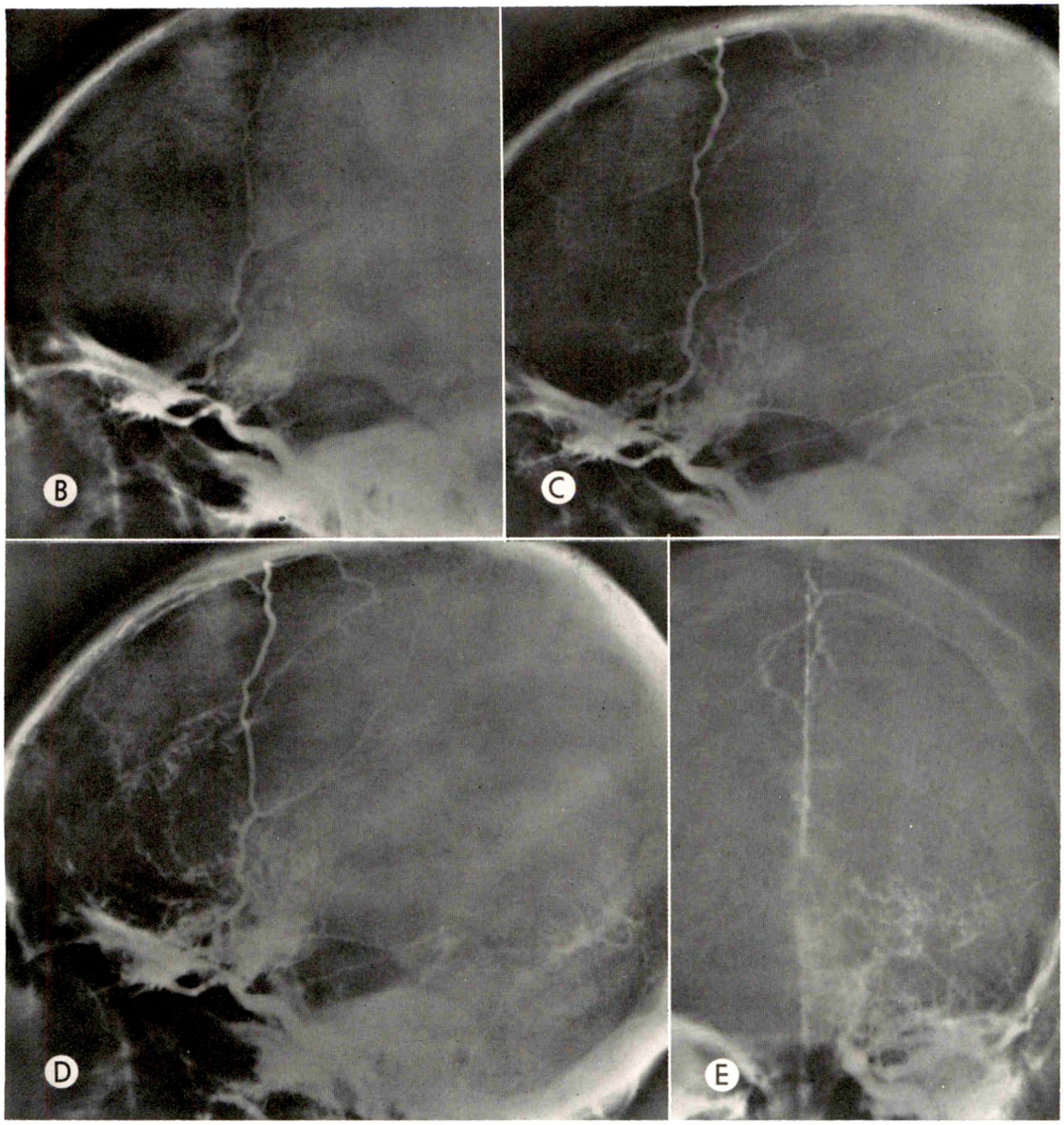


Fig. 8. (*B*, *C*, *D*, and *E*) Left carotid angiograms show occlusion of the internal carotid artery in the supraclinoid portion with a large anastomotic network in the region of the basal ganglia. The ophthalmic artery is markedly enlarged and shows a network of vessels evidently of the transdural anastomotic type. The middle meningeal artery arises directly from the ophthalmic artery in this case which is an uncommon anatomic variant (arrow in *B*). There is also enlargement of other meningeal branches arising from the internal carotid artery and supplying the tentorium (artery of Bernasconi and Casinari). The middle meningeal artery is seen to supply anterior cerebral branches by descending along the falx as demonstrated in the frontal projection in *E*.

external-internal carotid anastomoses (*rete mirabile*) is very well developed. In several of the cases, angiography demonstrated these anastomotic pathways quite well and yet the plain skull roentgenograms did not show appreciable widening of the middle meningeal and other meningeal artery grooves. Undoubtedly, if previous examinations were available for comparison, the enlargement would be noticeable. In none

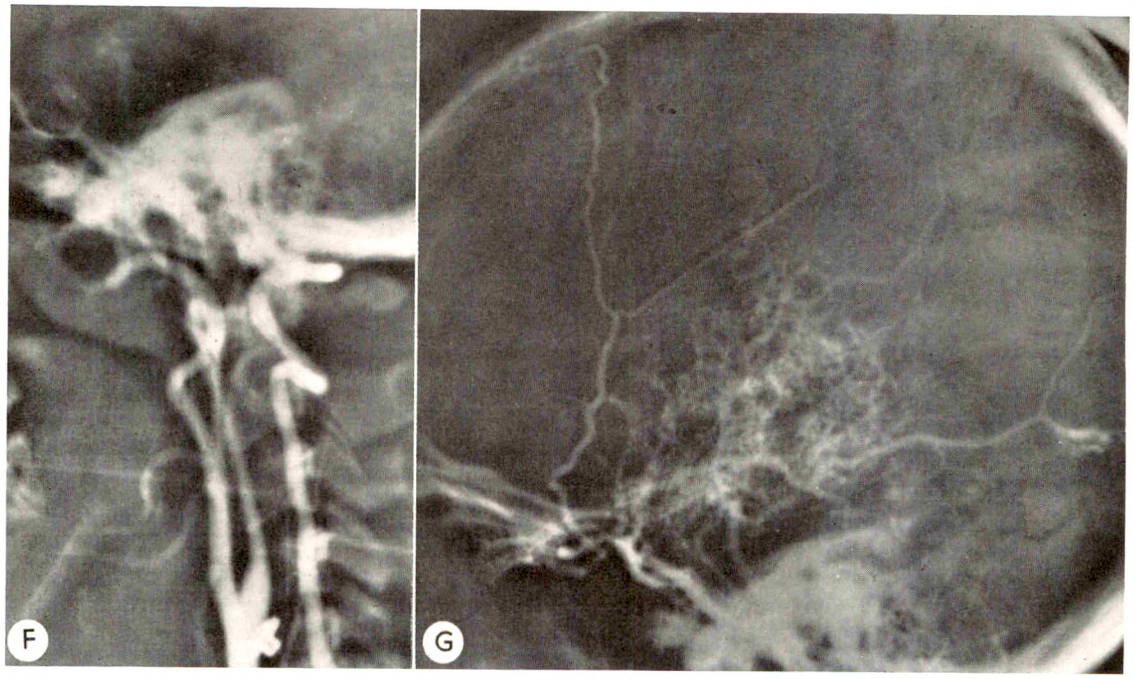


Fig. 8. (*F* and *G*) Right brachial angiograms demonstrate occlusion of the internal carotid artery in the supraclinoid portion and the usual tapering of this artery above the carotid bulb in the neck. The basilar artery is patent and there is a large spongy network of vessels arising from the posterior cerebral and posterior communicating arteries in the upper brain stem and basal ganglia region which eventually supply all of the middle cerebral artery territory as well as the anterior cerebral on both sides. There are also extensive external-internal carotid anastomotic groups (*rete mirabile*), both in the ophthalmic region and from the anterior and posterior branches of the middle meningeal artery.

of the cases reported here was there evidence of cerebral hemiatrophy with cranial hemihypertrophy such as is usually the case in children and adults some years following infantile unilateral hemiplegias. No calcifications were observed in any of the cases.

Cerebral angiography usually demonstrates the occlusion to be situated in the internal carotid artery at the bifurcation of

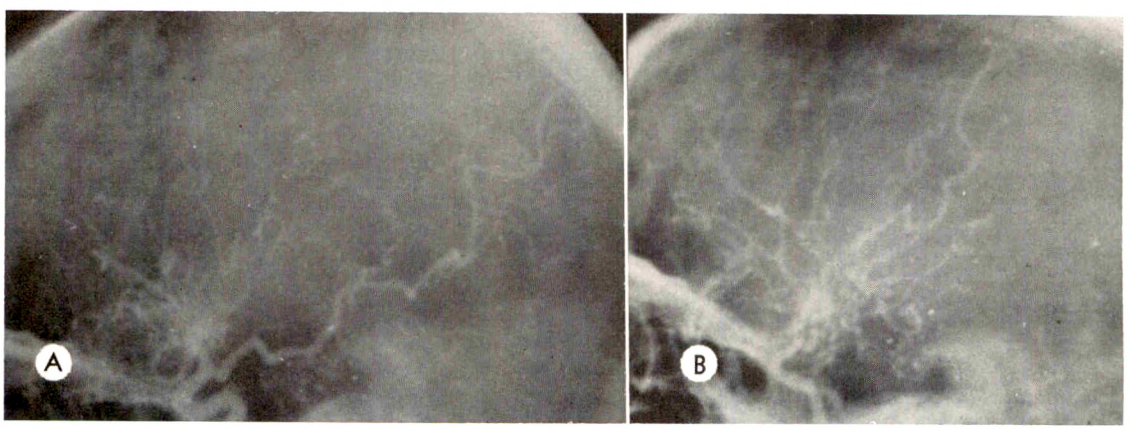


Fig. 9. Case x. (*A*) Left carotid and (*B*) right carotid artery angiograms demonstrate occlusion of the internal carotid artery in the supraclinoid portion with large basal network collateral formation. Eventually in the serialogram the intracranial branches filled fairly adequately on both sides.

this vessel. In the 2 instances where an angiogram was obtained *early*, a very localized narrowing of the internal carotid artery at the bifurcation involving the 3 vessels (internal carotid, anterior cerebral, and middle cerebral arteries) was observed (Fig. 4; and 6). I feel that this is a feature of this syndrome and it is probable that later the occlusion of the internal carotid artery could progress proximally to a certain extent but not below the level of the ophthalmic artery.

A remarkable finding in this disease process is the extraordinary development of a large network of fine vessels in the region of the basal ganglia and the upper brain stem arising from the carotid artery trunk, from the posterior communicating artery, from the basilar artery, and from the trunk of the anterior and middle cerebral arteries when partial filling of these is obtained. Why is there such pronounced development of these vessels in this condition when this is not usually the case in other single or multiple occlusive lesions? I believe that the answer lies in the fact that there is a progressive occlusion of the vessels starting at the bifurcation of the internal carotid artery and extending to involve the trunk of the anterior and middle cerebral arteries. Sometimes the posterior communicating and proximal portion of the posterior cerebral arteries are involved and in some cases the basilar artery is also occluded. Under these circumstances, the circle of Willis is affected early and cannot be used as a collateral pathway to supply the region of the basal ganglia, inasmuch as most of these perforating branches arise from the components of the circle of Willis and from the trunk of the middle cerebral artery. Consequently, those perforating branches which remain patent become considerably dilated and serve as a collateral pathway. Recanalization of the arteries at the base seems to occur but the lumen is extremely narrow in those cases that have come to autopsy. While there are no apparent direct end-to-end anastomoses of lentriculostriate arteries, the arteriolar-capillary network does communicate freely in this region. It is also evident that when the disease process starts early in childhood or during infancy, the development of the network in the base of the brain is apt to be greater.[52] Nevertheless, extensive networks are seen in the adult as well, although none as prominent as those that I have seen in children (Fig. 2; 7; and 9). The involvement of the circle of Willis has been emphasized by Kudo.[28] Another prominent angiographic feature is the visualization of the transdural external-internal carotid anastomotic pathways (*rete mirabile*), sometimes to a very marked degree (Fig. 1; 3; 5; and 9). The greatest degree of development of these collaterals was present in those cases that had basilar artery or posterior cerebral trunk involvement.

With the exception of 1 case (Case VIII), no lesions suggestive of atherosclerosis were observed angiographically in this group of cases.

COLLATERAL CIRCULATION

Because the trunks of the internal carotid artery as well as the anterior and middle cerebral arteries are occluded in these cases while the basilar artery may remain patent, collateral flow by way of end-to-end anastomoses on the surface of the cerebral hemispheres, both along the outer and inner surface,[48] is almost a constant finding unless there is occlusion of the basilar artery.

The most striking source of collateral flow in these cases is that afforded by the large network of vessels in the region of the basal ganglia from which contrast material filled practically all of the branches of the middle and anterior cerebral territory during serial angiography. In some cases the anastomoses between the anterior and posterior choroidal arteries have been very prominent.

The third important source of collateral supply in these cases is that of the transdural external-internal carotid anastomoses (*rete mirabile*) which were first described angiographically by Mount and

Taveras.[35] The fact that the circle of Willis is mostly occluded in these cases is no doubt a factor in the frequency with which the transdural anastomoses are observed. The development is particularly pronounced in those cases where basilar artery occlusion is present. A great number of different locations and configurations for these anastomotic pathways were encountered in this series of cases. Thus, in addition to the middle meningeal artery channels, those of other meningeal arteries arising from the vertebral and the occipital arteries were seen. Also, meningeal branches arising from the ophthalmic via the lacrimal and anterior meningeal arteries, as well as branches arising from the proximal portion of the internal carotid syphon, and in a few instances from the superficial temporal artery, were observed. These are illustrated in Figures 1, 3, 5, 7, and 8. It is of particular importance to note that in 1 of our cases (Case VIII) a subdural hematoma which became rather large within a period of 6 hours was seen. This followed ventriculography at which time a fair amount of air leaked into the subdural space (Fig. 7). The arteriography which had been performed a few days prior to ventriculography had demonstrated transdural anastomoses. Undoubtedly, the separation of the brain resulting from the subdural air resulted in rupture of some of these vessels which had already become enlarged to serve as collateral channels. Indeed, it is not unlikely that many subdural hematomas occurring after trauma are not due to rupture of veins along the sagittal sinus, but to shearing of these preexisting transdural arterial channels which in the ordinary case are quite small. Perhaps this factor (*i.e.*, arterial *versus* venous source of bleeding) may affect the behavior of subdural hematomas. This has not been hitherto considered as a common source of subdural hematomas in head trauma. At least 1 case in the literature affected by the syndrome discussed in this presentation died of a "spontaneous" subdural hematoma.[33]

NARROWING OF THE INTERNAL CAROTID ARTERY

The narrowing of the internal carotid artery below its point of occlusion in the supraclinoid portion down to a point just above the carotid bulb was an almost universal finding, but in some cases it was more pronounced than in others, the artery assuming a thread-like appearance. I believe that the degree of narrowing is related to the amount of flow through the artery and does not represent hypoplasia of this vessel such as has been suggested by some investigators.[31,42] Normally, perforating branches arise from the supraclinoid portion of the internal carotid artery, in addition to the anterior choroidal artery.[5] The ophthalmic artery as well as several small branches arise from the intracavernous portion of the internal carotid artery supplying the meninges in the region of the cavernous sinus and tentorium cerebelli. Sometimes these branches become quite large (Fig. 3; and 8) and would undoubtedly tend to maintain the lumen of the internal carotid artery open. In 1 of these cases (Case IX) the middle meningeal artery arose directly from the ophthalmic artery (Fig. 8). On the other hand, if flow from the internal carotid artery is much less, the internal carotid artery can become very thin (Fig. 4; and 7). It appears, therefore, that the narrowing of the internal carotid artery is an acquired phenomenon and not due to hypoplasia. In the cases where the occlusion of the internal carotid artery occurs very early in life or possibly even during intrauterine life, the intrapetrosal portion of the carotid artery will be correspondingly small, the carotid canal may be poorly developed and, in a few anatomic reports, absent.[17,23,27] If occlusion occurs early in life, however, underdevelopment is likely to result. Fisher[18] reports the case of a girl who died at the age of 17 years from an intracerebral hemorrhage, who had had a left hemiplegia at the age of 2 years with good recovery. The carotid canal of the petrous bone was extremely small and only large enough to permit the passage of the very thin internal

carotid artery. Undoubtedly, this patient had a supraclinoid internal carotid occlusion at the age of 2 years and the artery had become extremely small thereafter. The same phenomenon may be observed in the adult in the rare case where ligation of the intracranial portion of the internal carotid artery is carried out. The case shown in Figure 10*A* is that of a 52 year old man who had a suprasellar meningioma; upon surgical intervention the internal carotid artery had to be ligated. Angiography some 3 years later (Fig. 10, *B* and *C*) showed a diminutive internal carotid artery. The opposite may also occur. Figure 11, *A* and *B* demonstrates the case of a 17 year old girl who developed internal carotid occlusion in the supraclinoid portion. The internal carotid artery was very small, starting above the carotid bulb. Two

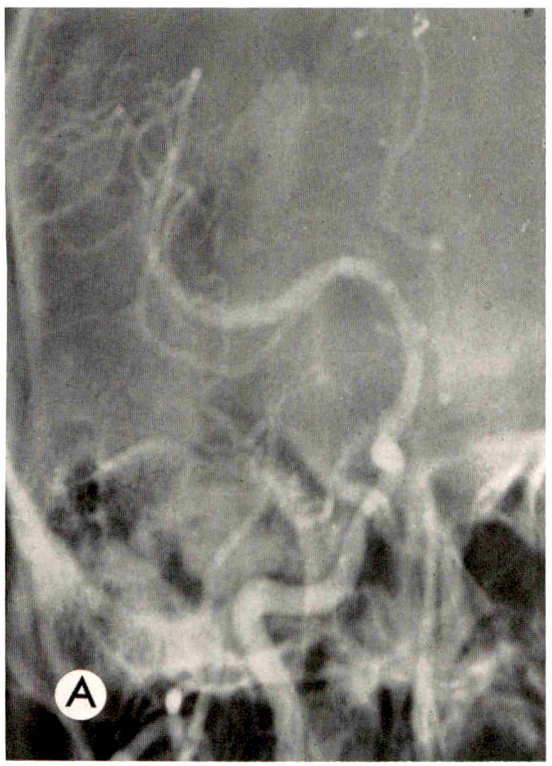
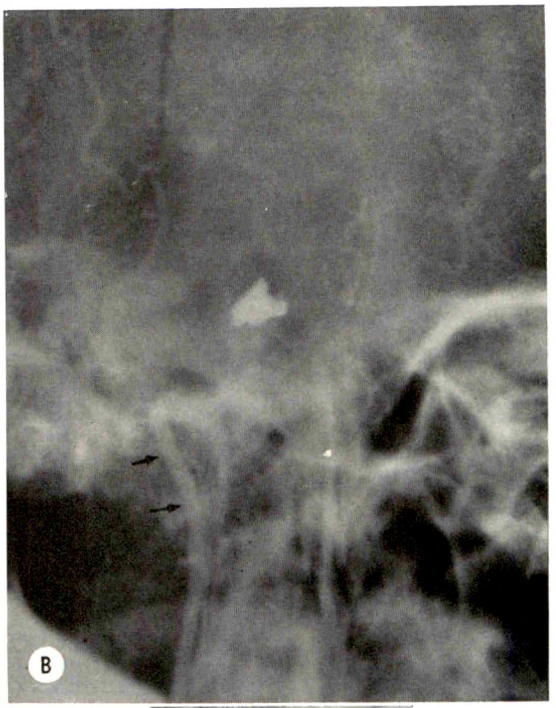


Fig. 10. (*A*) Frontal right carotid angiogram of a 52 year old man with a suprasellar meningioma. The tumor was wrapped around the vessel and ligation of the supraclinoid portion of the internal carotid artery became necessary during the surgical procedure.



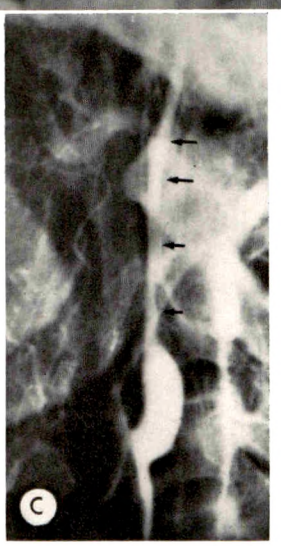


Fig. 10. (*B* and *C*) Right brachial angiograms 3 years later show considerable narrowing of the internal carotid artery below the metallic clips (arrows). In the lateral view it can be seen that the narrowing of the artery begins just above the carotid bulb (arrows) which is the usual location for the narrowing to start following occlusions of the internal carotid artery in the intracavernous or supraclinoid portions when there is decreased flow through branches of the internal carotid artery below the occlusion.

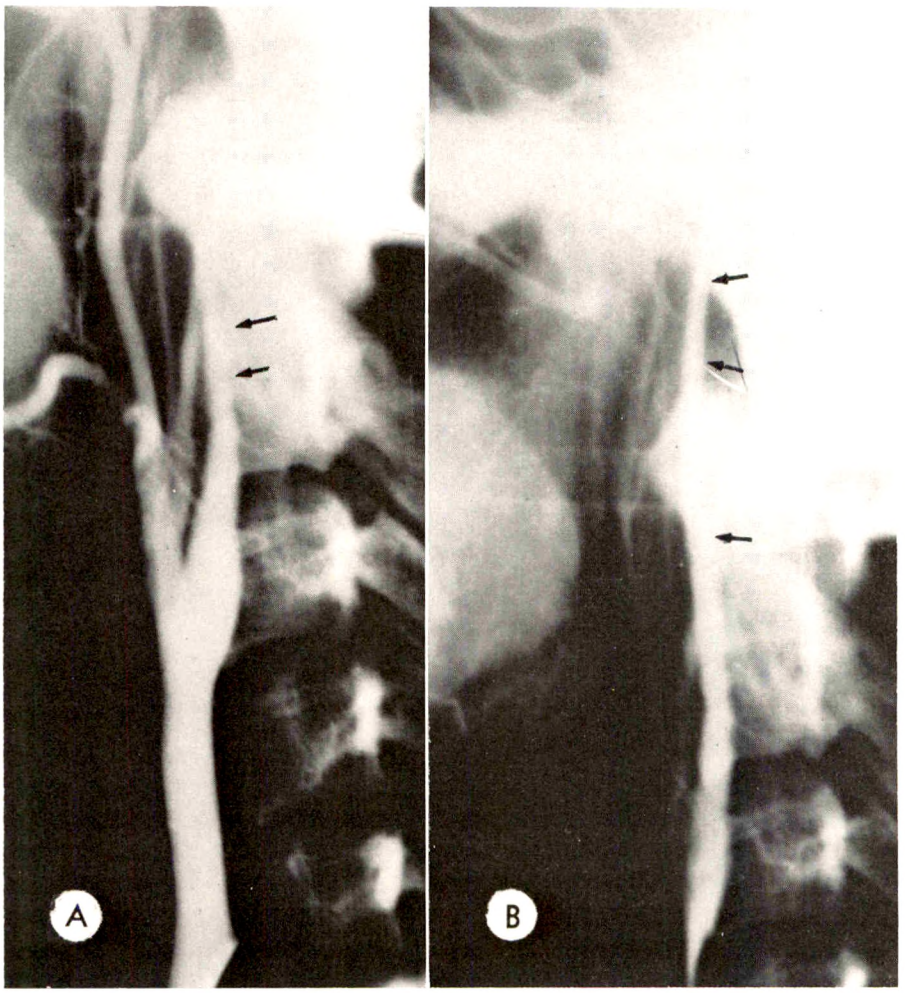


FIG. 11. (*A* and *B*) Right carotid angiograms in a 17 year old girl, who developed sudden hemiplegia, demonstrate marked tapering of the internal carotid artery (arrows) above the carotid bulb due to occlusion of this artery in the supraclinoid portion.

years later she returned with a subarachnoid hemorrhage at which time the internal carotid artery was found to be patent and extremely irregular in the supraclinoid portion due to recanalization. The size of the internal carotid artery was now more nearly normal (Fig. 11*C*).

It should be pointed out that if the internal carotid artery and, particularly, the middle cerebral artery are absent, the brain may not develop *in utero*.

REVIEW OF THE LITERATURE

Starting in 1964 and continuing into 1965, several reports appeared in the Japanese literature and a few in the American literature which correspond to the type of case that we are discussing here.[26,28,30,33,44,49,52] This year 2 reports appeared in the American literature by Japanese authors.[28,36] Kudo[28] reports 12 cases and Nishimoto and Takeuchi[36] report 96 cases collected by writing to various clinics in Japan. The latter probably includes Kudo's cases, but it is difficult to be certain how many were true examples of this syndrome. Of the 96 cases, 10 had the onset of symptoms before the age of 10 years, and 73 had the onset before the age of 21 years. They indicated that in patients over 20 years of age subarachnoid

hemorrhage was the most common onset. Only 2 of their collected group under the age of 21 years had subarachnoid hemorrhage. Only 4 of the total number of patients became progressively worse, 3 others died. Eight of their 96 cases were siblings (4 pairs). In the total of 96 cases collected by these authors, 55 were in female and 41 in male patients. There have been 3 autopsies reported (*vide infra*). Reference has been made above to the fact that bilateral internal carotid artery occlusions are not uncommon in the 6th and 7th decades of life, but in these cases the obstruction is in the initial segment of the internal carotid artery just above the bifurcation of the common carotid artery.[3, 12,15,16,22,45] The circle of Willis in these cases is intact and collateral flow is established by way of the basilar and posterior communicating arteries with the additional assistance of external-internal carotid anastomoses via the ophthalmic arteries. Occasionally, transdural external-internal carotid anastomoses (*rete mirabile*) develop in some of these cases, but only when the trunk of the middle or anterior cerebral arteries is also occluded.

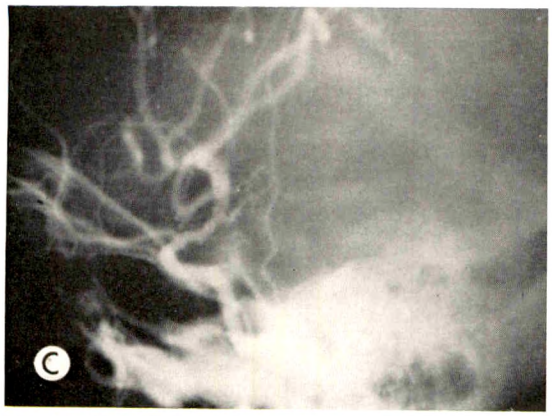


Fig. 11. (*C*) Repeat right carotid angiogram 2 years after the original examination when the patient returned because of a subarachnoid hemorrhage. The caliber of the internal carotid artery is nearly normal at this time and there is considerable irregularity in the supraclinoid portion, which is felt to indicate recanalization of the previously thrombosed vessel. There is also evidence of occlusion of major posterior branches of the middle cerebral artery. This case is *not* an example of the syndrome under discussion in this paper.

Infantile and childhood hemiplegias are usually unilateral and involve either the internal carotid artery in its intracranial portion, or the middle cerebral artery or its branches.[43,50]

The Japanese authors claim that this is a disease of the Japanese. In addition to the 96 cases collected by Nishimoto and Takeuchi,[36] the 2 cases reported by Leeds and Abbott[30] and 1 of the cases reported by Weidner and co-authors[49] were Japanese. One of the cases reported in this paper was Japanese. The remaining 8 cases, however, were not. One was a Negro from Haiti, another was an American Negro, and the remaining 7 were American white, all coming from different parts of the country. Judging from the reports in the literature, it is evident that the syndrome is more common in Japan. Although it is difficult to check on the accuracy of the diagnosis of many of the cases reported in the Japanese literature, the 12 cases reported by Kudo[28] appear to be genuine examples of this syndrome. I personally have seen at least 8 other cases which I cannot include in this report because, as expressed above, the studies were incomplete or there was some other feature that made inclusion unwise.

Etiology

Like many other vascular processes, the etiology of this condition is not known. It probably is not an atherosclerotic process because of the age in which it occurs and because of the absence of obstructive atherosclerotic lesions elsewhere in the body, although areas of atherosclerosis have been found in various arteries at autopsy. The localization of the disease process to the distal internal carotid artery and to the proximal anterior and middle cerebral arteries and, sometimes, the basilar and proximal posterior cerebral arteries, is remarkable.

There are very few autopsies where a careful study of the vessels was made.[26,33]

One case concerns a 9 year old girl who died of a subdural hematoma without trauma as a cause for it. Microscopically, the lumen of the arteries in the circle of Willis was very narrow but patent. Intimal thickening but no thickening of the media or adventitia and no inflammatory changes were encountered. In another case, a 12 year old girl, both internal carotid and both anterior and middle cerebral arteries were filled with grayish-black thrombi. Histologically the appearance was identical to the other case. In addition, this child had arteriosclerotic lesions in the common and external carotid as well as in some visceral arteries (liver, spleen, kidney). She also had lung and visceral tuberculosis; one kidney was "shrunk." The changes in the visceral arteries were said to be "similar" to those in the circle of Willis but less pronounced. In another autopsy reported by Suzuki *et al.*,[44] the findings at the base of the brain were distorted by an old tuberculous meningitis.

In view of the frequency with which children are affected by this condition, we must consider the possibility of an inflammatory process. Early reports indicate that damage to the arterial walls in children is not uncommon as a result of the effect of bacterial toxins in infectious diseases.[19] The problem is discussed in many publications dealing with infantile and childhood hemiplegia.[2,13,32,39] It is common to elicit a history of some type of nonspecific infectious process or "a cold" in the days or week preceding the development of the hemiplegia in children. In 18 of the 25 cases reported by Shillito,[39] there was a history suggestive of an infectious process or a cold preceding the development of neurologic findings.

Another cause for hemiplegia in the younger age group is dissecting aneurysm of the intracranial vessels.[39,50,51] Cerebral embolism is not uncommon in children and this may be associated with congenital heart disease. Septic emboli may lead to cerebral abscess formation in these cases. It is doubtful that cerebral emboli could explain this syndrome. Usually, cerebral emboli are propelled distally after partial lysis of the clot and usually dissolution takes place in time.[9,20,38] Trauma has been reported as a cause of post-traumatic occlusion in children.[11,14] However, it is not likely that trauma plays any part although the stress phenomenon caused by the moving blood striking the bifurcation of the internal carotid artery where an almost T-shaped configuration exists, may be an added factor in the localization of this disease process to this particular area. Radiation therapy may produce arterial changes and lead to thrombosis in children.[29] Other rare causes have also been reported in the literature.[7]

Multiple vascular occlusions can be seen in Marfan's syndrome involving the supraclinoid portion of the internal carotid arteries as well as the vertebral arteries.

There are some similarities between this syndrome and Takayasu's arteritis. However, Takayasu's arteritis is a disease of young females and involves only the aortic arch and the trunk of the major vessels, although a few cases have been reported where the abdominal aorta and some other abdominal branches have been involved. This is rare, however. Histologic evidence of involvement of muscular branches such as the coronary arteries has never been reported, which suggests predilection for arteries rich in elastic tissue. Judge and co-authors[25] emphasized in their discussion of the etiology of Takayasu's arteritis, the possibility that the disease may be an immunopathic reaction involving vascular elastin and also mention the possible importance of the hemodynamic stress in view of the localization in the aortic arch and trunk of major branches. Involvement of brain vessels intracranially is not encountered in Takayasu's arteritis in spite of the fact that in the original description of the disease, Takayasu, an ophthalmologist, described the changes in the eye. These changes, however, are somewhat nonspecific. They consist of transitory visual disturbances, cataract formation, arterio-

venous anastomoses, iris atrophy, retinal hemorrhages, microaneurysm, mydriasis, hyperemia of conjunctiva and sclera, enophthalmos, dilated retinal vessels, and retinal detachment.

Therefore, it is evident that, from the point of view of localization, the absence of involvement of the aortic arch and major vessels, and the age and sex distribution, the disease process being described here is not the same as that now known as Takayasu's arteritis.

On the other hand, it is difficult to escape the possibility that some type of non-specific inflammatory process plays a part.[45] Numerous cases of infantile and childhood hemiplegias, usually unilateral, have been seen by the present author. Some of them showed considerable vasodilatation in the region of the basal ganglia even in the acute stage in angiograms made a few days after the hemiplegia first appeared.[46] It is possible that in some cases follow-up angiography years later will show the vascular network typical of the cases being described in this paper. However, the instances of old hemiplegias with cerebral hemiatrophy that have come to my attention (at least 30 cases) have not had a well-developed vascular network. It is for this reason that I believe that the progressive syndrome described here is not the same disease process as that of infantile hemiplegias.

In 2 instances, the superficial temporal arteries were biopsied and were found to be normal. It appears that the syndrome under discussion is not related to giant cell arteritis.

DISCUSSION

It is clear from the summary of these cases that the age of onset is variable. It is also quite difficult to pin-point the time when the arterial occlusions began. In some cases, no symptoms or only vague symptoms suggestive of vascular episodes can be detected in the history even in adults. In young children, only paralysis or focal seizures can be used as evidence of the onset of this condition. The oldest patient was 42 years old when first studied and the youngest was 7 months in this group of cases.

An item worth discussing is whether the arterial lesions appear simultaneously or whether they appear in sequence. It seems that in most of the cases the development of the lesions takes place within a relatively short period of time, a few weeks to a few months elapsing between the development of bilateral signs. After the major intracranial vessels are occluded, the occlusive process seems to reach a plateau. The same feature was pointed out by Kudo.[28] The large branches of the middle cerebral artery usually remain patent and the occlusion only involves the trunk of the middle and anterior cerebral arteries. In Case II, the left anterior cerebral artery was open, although stenotic, in the region of the anterior communicating artery, but the right was occluded more distally, thus interfering with filling of the pericallosal artery which is probably why collateral channels developed in the region of the corpus callosum.

Some clinical features of this disease process are worthy of special mention. In addition to the alternating hemiparesis, alternating twitching movements or minor convulsions may be observed. Episodes of staring in space and dizziness were described. Headache was an unusually prominent symptom in 2 of the cases (Case II and VI) and a less important symptom in at least 2 others. Changes in mood, depression and hallucinations were a prominent feature in 2 cases (Case I and IV) which led to psychiatric treatment and in 1 case to admission to a mental hospital. A subarachnoid hemorrhage was encountered in 2 of the cases (Case II and X) and in another case (Case VII) there was a bloody spinal tap. However, a traumatic tap in this 7 month old infant could not be ruled out. An aneurysm was discovered in this case but it was situated in the opposite side to that where the original hemiplegia developed.

One of the frequent complications en-

countered in this disease process is intracranial hemorrhage which was encountered in at least 2 of the cases reported here and in 12 of 23 adults reported by Nishimoto and Takeuchi,[36] as well as in 2 of the children reported by these same authors. In my experience, I have encountered at least 2 other cases of intracranial hemorrhage occurring spontaneously in patients who had a history of hemiplegia with angiographic demonstration of occlusive lesions. It is likely that rupture of intracerebral network collaterals is responsible for these hemorrhages. Some of these network collaterals are deep in the basal ganglia region, but many of them are visible on the undersurface of the brain.[18]

SUMMARY AND CONCLUSIONS

Ten cases of a syndrome characterized by multiple progressive intracranial arterial occlusions are reported. The term progressive is used because of the clinical history, and the fact that, in a few instances, arteriographic findings indicating progression of these occlusive lesions were observed.

It appears that in the great majority of cases the lesions progress to complete obstruction of most of the major arterial channels along the base of the brain and then the process stops, so that most of the patients are able to lead a fairly normal life with only moderate disability and, in a few instances, with practically no disability. Mental retardation was present in about a third of the children.

In 1 instance (Case 11), the arteriographic findings seemed to progress on one side over a period of 2 weeks, but re-examination 4 months and 15 months later showed that the appearance had improved on this side. Unfortunately, it is difficult to be certain that the apparent progression and regression was due to the primary process and that it was not due to arterial spasm associated with a subarachnoid hemorrhage. In defense of the fact that this was not spasm may be stated that the angiography performed a few days after the alleged subarachnoid hemorrhage showed little arterial narrowing, whereas the one performed 10 days later showed progression and considerably more narrowing (Fig. 2). A question, therefore, may be raised as to whether these arterial lesions are capable of regression, and, if so, under what circumstances? Are they amenable to treatment by certain agents such as steroids? Only 1 patient in this group (Case v) received steroids rather late in the course of the disease, and showed no discernible benefit.

Clinically, these patients present symptoms and/or signs alternating between the right and left sides and in addition to paralysis may present convulsions, twitching movements, speech disturbance, unsteady gait, hemianopsia, etc. Headache was a prominent symptom in a few cases. Mental retardation may be an important feature in children. Psychiatric manifestations may be prominent when the disease process starts during adult life; 2 of the 10 cases had such manifestations. Spontaneous intracranial hemorrhage is a frequent occurrence in these cases probably due to rupture of the fine collateral channels.

A striking aspect of this disease process is that the distal branches of the anterior, middle, and posterior cerebral arteries are usually not involved, thus permitting an adequate flow to the brain cortex if the collateral circulation is adequate.

Filling of all the channels takes place by 3 main pathways: (a) the end-to-end anastomoses among the branches of the anterior middle, and posterior cerebral arteries over the surface of the brain (the so-called leptomeningeal arterial anastomoses) which were found to be an important source of collateral supply when the basilar artery was not occluded; (b) an extremely dilated network of thin vessels in the basal ganglia region which in some cases was sufficient to supply all of the branches of the middle and anterior cerebral arteries; and (c) the transdural external-internal carotid anastomoses (*rete mirabile*).

The etiology is unknown. Because children are so frequently affected and because the lesions progress to complete obstruction

of the major arteries within a relatively short period of time and then the process stops, the question of a nonspecific inflammatory process or possibly an autoimmune reaction must be raised, although in the few autopsied cases no inflammatory lesions were seen in the arterial wall.

The fact that one of our patients developed a large subdural hematoma following ventriculography with leakage of air into the subdural space, and that at least one other case in the literature was reported as dying of a "spontaneous" subdural hematoma, raises the question as to whether rupture of these transdural anastomotic channels may not be an important cause of post-traumatic subdural hematomas even in patients not affected by obstructive intracranial vascular lesions leading to enlargement of these arterial channels.

I believe that the cases just described represent examples of a cerebral vascular occlusive syndrome which is different from the infantile hemiplegias and entirely different from the bilateral carotid artery occlusions secondary to atherosclerosis usually encountered in the later decades of life.

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AN UNUSUAL COMPLICATION OF CEREBRAL ANGIOGRAPHY*

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ANGIOGRAPHIC visualization of the cerebral vessels is a commonly performed procedure in the diagnosis of both vascular and nonvascular lesions of the cranium. The method most commonly used is percutaneous needle puncture of the common carotid artery in the inferior portion of the neck, a technique originally described by Loman and Myerson in 1936.[8]

Selective catheterization of the internal carotid artery for the performance of cerebral angiography, however, presents certain advantages over simple needle puncture of the common carotid artery. Selective internal carotid artery catheterization can be performed either by the Seldinger[12] catheter technique of replacing the needle by a plastic catheter or, alternatively, by advancing the needle itself over the guide wire into the internal carotid artery.[2] Using the latter technique the authors encountered what appears to be a unique complication of cerebral angiography—namely, a fracture of a plastic guide wire and distal embolization of the fractured segment with its lodgement in the internal carotid artery just proximal to the carotid siphon. The rarity of this type of complication and its method of management prompted this report.

REPORT OF A CASE

A 43 year old white male was admitted to this hospital for investigation of severe frontal and parietal headaches of many years' duration. Four years prior to admission the patient had an episode of left hemiparesis which gradually cleared over a 6 month period. For 2 weeks prior to admission the headaches had become more severe and intractable.

On physical examination the blood pressure was 140/100, the pulse 96/minute and regular, the respiratory rate 20/minute and the temperature 98°F. Abnormal findings were limited to the neurologic system. There was diminished sensation to pin-prick over the left side of the face with a decrease in the left corneal reflex and left facial weakness of the peripheral type. There was impairment of rapid movement of the left hand and left foot with weakness of the triceps muscle of the left arm and the extensor muscles of the left wrist. There was also impaired pin-prick and vibration sensation over the left upper and lower extremities. The possibility of an arteriovenous malformation was considered and the patient was referred for investigation.

On October 1, 1965 right carotid arteriography was attempted under general anesthesia. A Cournand needle was inserted into the right common carotid artery without difficulty and a good back-flow of blood was obtained. A plastic guide wire was passed through the needle and the needle threaded over the wire into the internal carotid artery. When the guide wire was removed slight resistance was encountered and inspection of the guide wire revealed that the barium impregnated radiopaque tip of the wire was missing. Roentgenography of the skull demonstrated the foreign body in the long axis of the internal carotid artery in the petrous portion of the temporal bone just proximal to the carotid siphon (Fig. 1). When the complication was recognized, the procedure was abandoned, the needle removed from the carotid artery and the patient aroused from the anesthetic. When he was conscious a careful neurologic examination failed to reveal any additional neurologic deficit that had not existed prior to anesthesia.

Two hours after the first procedure the patient was again anesthetized and systemic hypothermia was induced with a cooling blanket supplemented with ice-packs to the axillary and inguinal regions. A catheter was placed in the right radial artery to monitor arterial pressure. An oblique incision was made along the anterior border of the sternomastoid muscle and the common, external and internal carotid ar-

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FIG. 1. Roentgenogram of the skull performed following removal of the needle from the common carotid artery demonstrates the foreign body (arrow) in the distal internal carotid artery.

teries isolated. With the rectal temperature lowered to 30°C. and the systolic blood pressure artificially maintained at 180 mm. Hg systolic with the aid of an intravenous infusion of phenylephrine, an arteriotomy was performed on the internal carotid artery just distal to the bifurcation. Attempts at dislodging the foreign body by retrograde bleeding from the distal internal carotid artery were unsuccessful. After a 2 minute period of occlusion of the common carotid artery, the arteriotomy in the internal carotid artery was closed with a partially occluding vascular clamp and circulation to the brain restored. Several additional unsuccessful attempts to obtain the foreign body were made in this manner. Attempts at removal of the foreign body by passing small grasping forceps through the artery were also unsuccessful. Red rubber catheters and ureteral catheters were likewise used unsuccessfully, as were embolectomy balloon catheters. After approximately a dozen attempts by these various maneuvers, a repeat skull roentgenogram demonstrated that the foreign body had not changed its location. A final attempt was then made to extract the foreign body with a small right-angled metal sucker tip, an instrument used by otolaryngologists for aspirating blood during tonsillectomy. The sucker tip was passed into the artery as far as possible and on withdrawing the instrument the foreign body was disloged and descended adjacent to it (Fig. 2). The arteriotomy was closed and the patient rewarmed. The postoperative course was completely uneventful and the patient was discharged on the sixth postoperative day. He remains well in the follow-up period with no change in his neurologic status.

DISCUSSION

The conventional needle technique for cerebral angiography involves puncture of the common carotid artery in the neck with injection of the contrast agent through the needle. When performed in this manner the procedure is subject to a number of complications. Subintimal or intramural contrast material injections are not rare occurrences and may result in thrombosis of the vessel with an occasional fatality. Rimpau and Seils[9] studied 200 autopsy cases who had undergone previous carotid puncture by the needle technique and demonstrated intramural hematoma with varying degrees of vascular occlusion in 8 per cent of these cases. Saltzman[10] reported extravascular injections in 10 per cent of 1,020 cases using this conventional technique.

Selective catheterization of the internal carotid artery by the Seldinger catheter technique[12] has been carried out by Liverud,[7] Elfvin,[3] Schechter,[11] Amundsen *et al.*[1] and Hanafee and Weidner.[4] The advantages of such a technique include a reduction in the number of intramural and extravascular injections, the use of smaller volumes of contrast medium and the elimination of overlapping of the internal and



Fig. 2. The foreign body following its removal and the instrument used to remove it.

external carotid arteries. However, using this technique, the rate of cervical hematomas appears to be relatively high.

Bergstrand[2] described an improved technique for selective internal carotid arteriography whereby the common carotid artery is punctured by a blunt cannula fitted with a sharp needle. The needle is then removed and following a test injection through the cannula, a guide wire is inserted into the internal carotid artery through the cannula; the cannula is then advanced over the guide wire. Bergstrand[2] reported the use of this technique in 65 cases without a single complication. This was the technique used in the reported case and represents the only complication of the technique in this hospital.

Techniques involving the use of guide wires or catheters are associated with another potential hazard; namely, guide wire or catheter fracture and embolization of the fractured segment in the arterial tree. Fortunately, this is a rare complication of this type of angiographic technique. Kottke and co-workers[5] reported this complication only once in 195 abdominal aortographies performed by the percutaneous transfemoral route. Lang,[6] in a survey of 142 urologists, radiologists and vascular surgeons, was able to evaluate 11,402 cases of percutaneous retrograde arteriography performed by the Seldinger technique. There were 5 instances in which the catheter tip or guide wire fractured during catheterization and became embedded in the intima or adventitia of the large vessel. All were successfully removed surgically.

The plastic guide wire used in our case contained an inner wire which extended up to but not into the distal barium impregnated radiopaque segment. In other words, the radiopaque tip consisted only of plastic. As the guide wire was withdrawn through the cannula of the Cournand needle, the plastic segment was sheared from the remainder of the guide by the sharp edge of the cannula. Because of this potential hazard we no longer use this type of guide wire.

Removal of the foreign body from the distal internal carotid artery presented a special problem, since the foreign body could not be approached directly and had to be removed through an arteriotomy situated at some distance from the object itself. The problem was further compounded by the lack of any specific instruments by which the object could be grasped. Systemic hypothermia and elevation of the blood pressure with the vaso-

pressor phenylephrine provided increased protection to the brain during the multiple periods of carotid occlusion.

SUMMARY

Fracture of the tip of a plastic guide wire occurred during the performance of selective internal carotid angiography. The embolized tip was successfully removed from the distal internal carotid artery with the aid of systemic hypothermia and artificial maintenance of an elevated blood pressure. Fortunately, this is a rare complication of angiography and can be reduced in frequency by meticulous attention to detail and careful examination of equipment prior to the performance of the procedure. The potential hazard of the plastic guide wire in this case is emphasized.

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ANATOMIC VARIATION OF THE HEIGHT OF THE FALX CEREBRI*

ITS RELATIONSHIP TO DISPLACEMENT OF THE ANTERIOR CEREBRAL ARTERY IN FRONTAL SPACE-OCCUPYING LESIONS

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A SUPRATENTORIAL space-occupying lesion can be diagnosed at carotid angiography by its abnormal circulation or, when this is lacking, by the type of dislocation of arteries and veins it produces. Displacement of the anterior cerebral artery and its branches across the midline represents one of the main features of carotid angiography and its aspects greatly contribute to the diagnosis. It is well known that the shift of the anterior cerebral artery assumes the form of a rounded arc in a case of frontal expansive lesion, and that of a square when the space-occupying lesion is posteriorly placed.

Tumoral angiographic picture, however, may occasionally present characteristics which are somewhat different from those considered as typical of expansive lesions of similar size and location. We have observed, for example, cases of frontal expansive lesions producing a square shift of the anterior cerebral artery, which is considered typical of posterior lesions. In most of the cases these abnormal findings can be related to the degree of cerebral edema accompanying the lesion as well as to its nature and to the peculiarity of its location and development. In some cases, however, the explanation of the abnormal angiographic picture can be found in anatomic variation of the intracranial structures which may have a significant relation.

It can be conjectured that the type of dislocation across the midline of the anterior cerebral artery and its branches may depend, besides the well known factors, on the amplitude of the "hernial hiatus" delimited by the falx and the corpus callosum through which herniation occurs. By the peculiarity of its anatomic relationship to the anterior cerebral vessels, a large hernial hiatus represents a condition predisposing to a rounded shift of these arteries, while a narrow hernial hiatus favors a displacement of the square type. Since variations in shape and size of the anterior part of the corpus callosum are minimal,[3] the height of the falx cerebri can be considered the main factor in determining the amplitude of the hernial hiatus.

The present study was aimed (1) at investigating anatomic variations of the height of the falx cerebri, and (2) at evaluating the importance of these variations in determining different types of displacement of the anterior cerebral artery in frontal expansive lesions.

MATERIAL AND METHOD

This study is based on 200 selected carotid angiographies of adults where the inferior longitudinal sinus was visualized in lateral projection. Since this sinus is placed in the posterior two thirds of the free margin of the falx,[1] its position served to evaluate the height of the falx cerebri at different points. Krayenbühl and Yaşargil[2] found that the inferior longitudinal sinus comes into view in about 59 per cent of carotid angiographies.

Various measurements were made in the venous phase of carotid angiography in the lateral view, as shown in Figure 1, in order to evaluate the height of the falx at different points. Also, measurements of the

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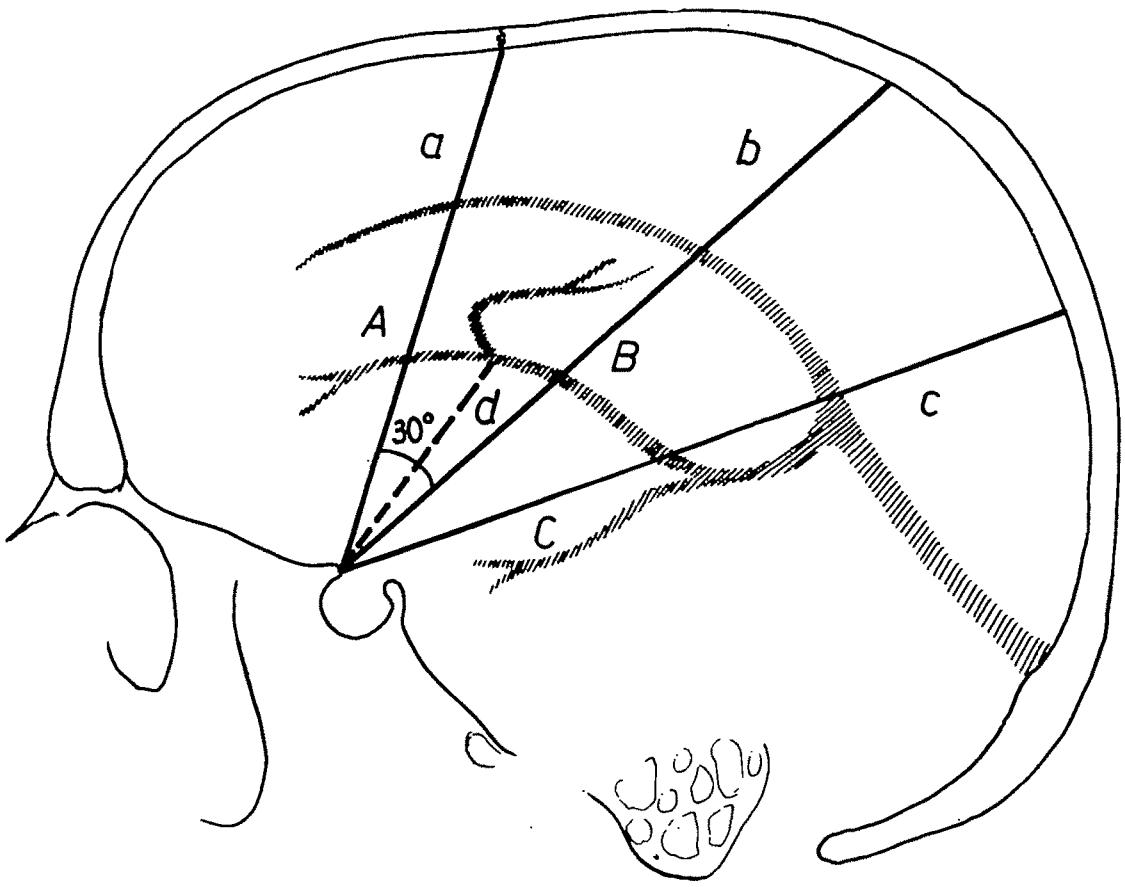


FIG. 1. Schematic drawing showing the technique of measurements.
A. Distance between the tuberculum sellae (ts.) and the internal surface of the skull at the bregma.
(a) Distance from the internal surface of the skull to the inferior longitudinal sinus (ils.) along line A.
B. Distance between the tuberculum sellae and the internal surface of the skull forming an angle of 30° posterior to line A.
(b) Distance from the internal surface of the skull to the ils. along line B.
C. Distance between the ts. and the internal surface of the skull along a line crossing the proximal end of the vein of Galen.
(c) Distance between the internal surface of the skull and the ils. along line C.
(d) Distance from the ts. to the venous angle where the thalamostriate and septal veins join the internal cerebral vein.

height of the venous angle and of the height of the skull were made searching for their possible relationship to falx size.

In addition, 3 cases are presented of frontal glioma verified at surgery, with masses of similar size and corresponding location, which showed different types of anterior cerebral shift.

RESULTS

The results of falx measurements are summarized in Table 1. Frequent and sometimes marked individual variations in the height of the falx cerebri were found, ranging from 28 to 48 mm. anteriorly, from 41 to 62 mm. at the middle and from 40 to 62 mm. at the posterior points.

The height of the falx was compared with the corresponding height of the skull measured from the tuberculum sellae, but no significant relationship was found between the two categories of measurements. Similarly, no relationship was detected between the height of the falx and the distance of the

Table I

ANATOMIC VARIATION OF THE HEIGHT OF THE FALX CEREBRI

	Minimal (cm.)	Maximal (cm.)	Mean (cm.)
Distance from tuberculum sellae to bregma (A)	8.6	11.5	9.9
Distance from ts. to skull (B)	10.5	13.8	8.19
Distance from ts. to skull (C)	11.3	14.3	11.2
Height of falx cerebri in (a)	2.8	4.8	3.58
Height of falx cerebri in (b)	4.1	6.2	5.19
Height of falx cerebri in (c)	4.0	6.2	5.27
Distance from ts. to venous angle (d)	3.2	5.5	3.54

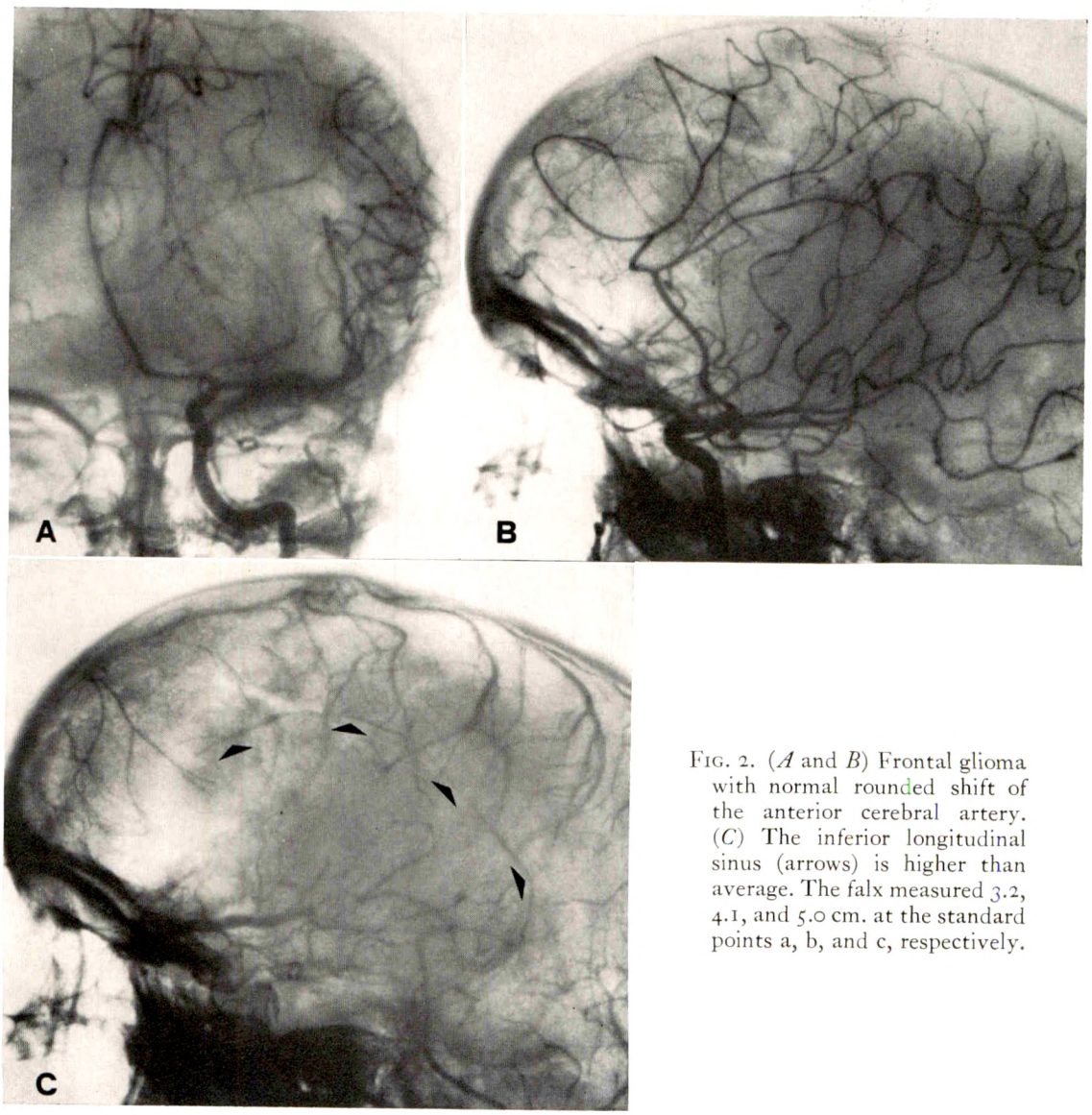


Fig. 2. (*A* and *B*) Frontal glioma with normal rounded shift of the anterior cerebral artery. (*C*) The inferior longitudinal sinus (arrows) is higher than average. The falx measured 3.2, 4.1, and 5.0 cm. at the standard points a, b, and c, respectively.

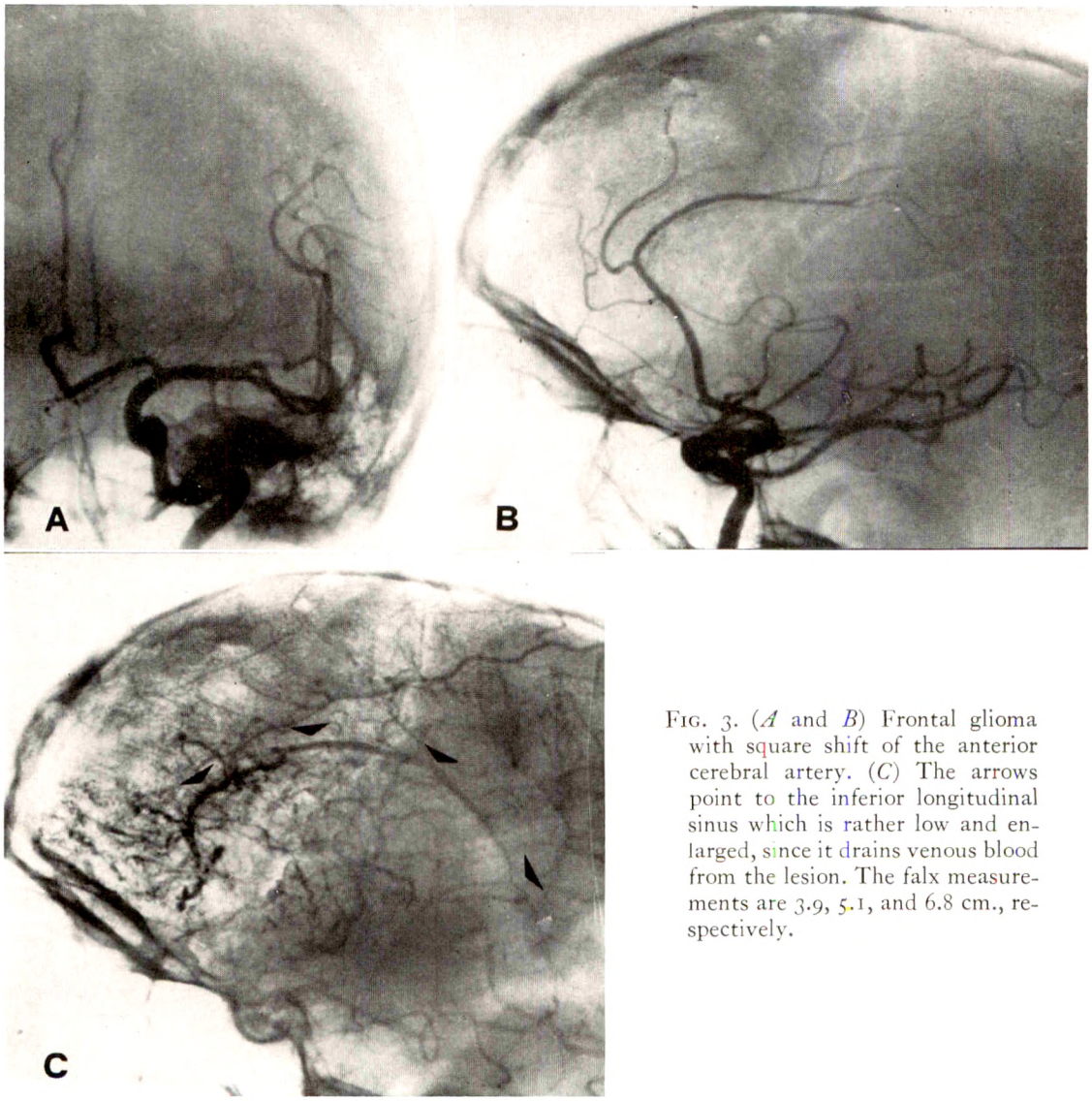


FIG. 3. (*A* and *B*) Frontal glioma with square shift of the anterior cerebral artery. (*C*) The arrows point to the inferior longitudinal sinus which is rather low and enlarged, since it drains venous blood from the lesion. The falx measurements are 3.9, 5.1, and 6.8 cm., respectively.

venous angle from the tuberculum sellae, ranging from 32 to 54 mm.; a low venous angle was not associated with a large falx and, *vice versa*, a high venous angle was not related to a narrow falx.

These measurements bring into evidence the primary variation in the size of the falx, independently of skull dimensions, and thus of the interspace between the falx and the corpus callosum. Consequently, different amplitudes of the hernial hiatus may contribute to explain the various types of anterior cerebral artery shift in cases of frontal expansive lesions.

One of the 3 cases presented showed a rounded shift of the anterior cerebral artery (Fig. 2, *A–C*), while the other 2 exhibited a square shift (Fig. 3, *A–C*; and 4, *A–C*). In the case with typical, rounded shift the falx measurements were 32, 41, and 50 mm. at the anterior, middle and posterior points, respectively, which are below average, indicating a large hiatus. The cases with abnormal, square shift had a rather

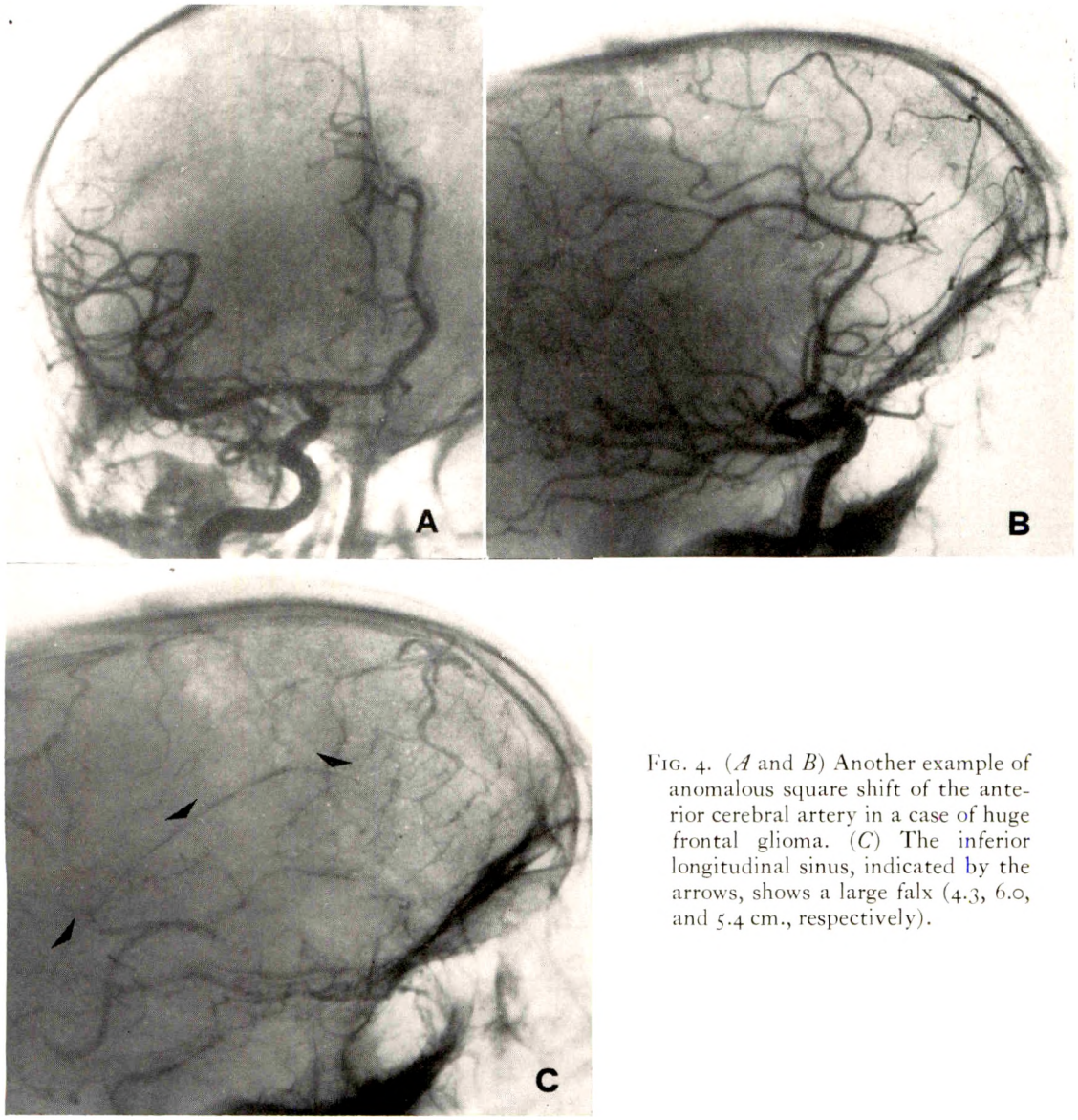


Fig. 4. (*A* and *B*) Another example of anomalous square shift of the anterior cerebral artery in a case of huge frontal glioma. (*C*) The inferior longitudinal sinus, indicated by the arrows, shows a large falx (4.3, 6.0, and 5.4 cm., respectively).

large falx, showing measurements of 39, 51, and 68 mm.; and 43, 60, and 54 mm., respectively, well above average, which narrowed significantly the hiatus.

Similar abnormal features have been observed in several other cases.

It thus appears that when the falx is large, the possibility of displacement of the anterior cerebral artery across the midline is limited by a narrow hiatus. The resulting shift of a frontal expansive lesion is a limited arc with steps at one or more points, similar to the square shift of posterior lesions.

Conversely, if the hiatus is large, it is possible that even posterior lesions may cause anterior cerebral artery shift with rounded arc and no steps at any arterial segment, similar to that observed in frontal expansive lesions. This remains hypothetical, however, as we have not seen such a picture as yet.

These observations are not intended to ascribe the height of the falx cerebri and related cerebral artery shift a particular, definite value. A correct diagnosis must be based upon several factors and not limited to a single angiographic picture. However, knowledge of the various elements that may influence the type of dislocation of the anterior cerebral artery across the midline is useful and contributes to a better understanding of abnormal angiographic pictures whose interpretation may seem uncertain and difficult at first sight.

SUMMARY

Differences in the height of the falx cerebri are demonstrated.

Abnormal anterior cerebral artery shift of frontal space-occupying lesions may be related, besides the well known factors such as degree of coexisting edema and peculiar location of the lesion, to these anatomic variations of the falx cerebri.

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Vol. 106, No. 2

TRAUMATIC ARTERIOVENOUS FISTULA OF THE SUPERFICIAL TEMPORAL ARTERY*

REPORT OF A CASE

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THERE is a paucity of material in the angiographic literature regarding traumatic lesions of the superficial temporal artery, with only 2 cases of pseudoaneurysm[8,20] and a single case of arteriovenous fistula[1] of this vessel having been demonstrated angiographically.

In 1935 Winslow and Edwards[18,19] collected from the literature 18 cases of posttraumatic arteriovenous aneurysms of the superficial temporal artery. The earliest case recorded by these authors in their series was one reported in 1828 by Green.[7] These patients experienced a buzzing or

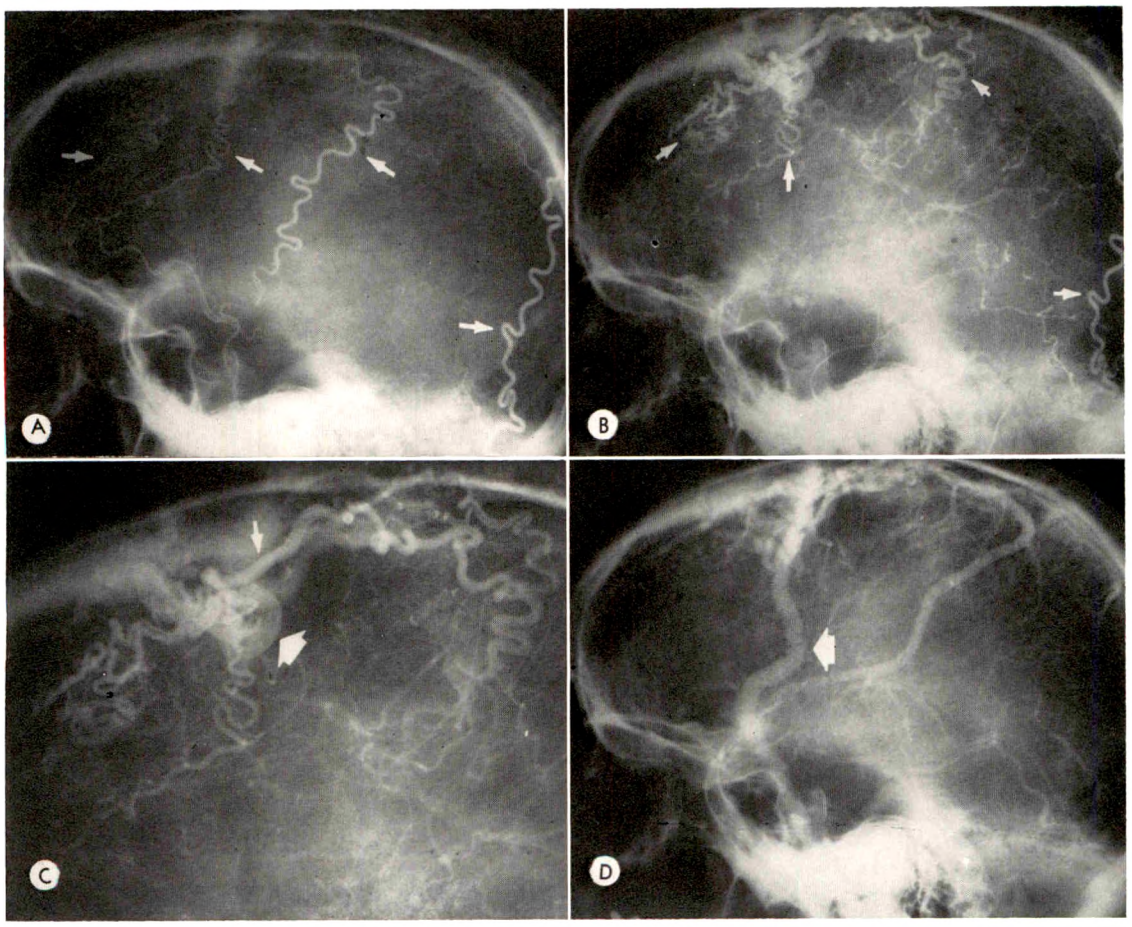


FIG. 1. Right external carotid arteriograms. (*A*) Branches of the superficial temporal artery (upper arrows) and occipital artery (lower arrow) are demonstrated. (*B*) Late arterial phase. There is filling of the arteriovenous fistula fed by the superficial temporal and occipital arteries (arrows). (*C*) Details of the arteriovenous fistula. Major feeding artery (small arrow) and venous drainage (large arrow) are shown. (*D*) Venous phase. There is venous drainage via the superficial temporal vein (arrow).

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hissing sound in the ear on the side of the lesion and frequently complained of headaches and dizzy spells. Physical examination revealed primarily a pulsatile mass along the course of the superficial temporal artery with tortuous vessels in the preauricular area. Subsequent additional cases of traumatic arteriovenous fistula[9] and pseudoaneurysm[2–6,10,12,13,15] of the superficial temporal artery have appeared in the literature, but without angiographic documentation.

REPORT OF A CASE

A 28 year old Indian male was admitted to his local hospital July 12, 1967 immediately following an automobile accident. The patient was unconscious and had sustained an L-shaped laceration of the right frontotemporal scalp. The laceration was sutured and the patient remained in the hospital for 2 weeks. No neurologic deficit was noted nor was a skull fracture demonstrated roentgenographically. He returned to work in February of 1968.

In May of 1968 he noticed intermittent swelling of the right frontotemporal area, particularly when bending forward. This was accompanied by headaches and a buzzing noise in the right ear with occasional dizzy spells.

The patient was admitted to this hospital September 3, 1968. Physical examination revealed a pulsatile vascular mass measuring 1 ×3 cm. in the right frontotemporal area of the head. There was a loud bruit over the mass when he bent forward. There were varices of the preauricular region on either side of the head which also became more prominent on bending forward. The bruit disappeared with right temporal artery compression. No other abnormalities were noted.

On September 4, 1968 right percutaneous external carotid arteriography demonstrated that the frontal and parietal branches of the superficial temporal artery as well as the occipital branch of the external carotid artery converged to a point, with subsequent filling of several sinusoids (Fig. 1, *A*, *B*, and *C*). Venous drainage to the right superficial temporal vein was present (Fig. 1*D*). Right percutaneous internal carotid arteriography showed no abnormalities of the intracranial circulation.

A left carotid arteriogram demonstrated that the frontal and parietal branches of the superficial temporal artery also fed the fistula on the right, with venous shunting into the right superficial temporal vein.

At surgery, the arterial and venous connections of the fistula were identified and the vessels were ligated. The entire fistula was then excised.

Postoperatively the patient did well and was discharged on September 10, 1968.

Comment. Lesions in the distribution of the external carotid artery are best demonstrated by selective external carotid arteriography.[11,14,16,17]

SUMMARY

A case of traumatic arteriovenous fistula of the superficial artery following a laceration of the frontotemporal scalp is reported. The fistula was demonstrated angiographically by means of selective percutaneous external carotid arteriography.

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ULTRASONIC CAROTID ECHOARTERIOGRAPHY*

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TODAY, strokes are the third most frequent cause of death in the United States and most of the other "developed" countries. Furthermore, another two million Americans, of whom one-third were wage earners prior to their stroke, have felt to some extent the physical, mental and financial burden of this disease. As life expectancy continues to increase, morbidity and mortality from cerebrovascular disease will continue to increase.[3]

The majority of stroke patients show blockage or narrowing of the carotid bifurcation or of the origin of the vertebral artery by atherosclerosis on four-vessel angiography, as reported by the Joint Study on Arterial Occlusion and by other investigators.[12,13] To screen patients for vascular surgery, four-vessel angiography has been essential, but this method has a number of drawbacks in that it entails pain and risk, requires hospitalization, requires expensive roentgenographic equipment and skilled personnel. Also, it failed to show an operable lesion in 25 per cent of the cases, is not suited for repeated studies in longterm evaluation of surgical results or the objective assessment of the effectiveness of drugs, diets, or gastric shunting procedures in reversing or preventing atherosclerosis.[3,13,15] What is needed is a safe and simple pre-stroke screening system to visualize extracranial vascular disease.[3] Since reconstructive arterial surgery is reported as safe and effective in preventing transient ischemic attacks or the so-called "little strokes," in contrast to a high mortality and morbidity in patients with acute and progressive strokes,[4,5,13,27] corrective surgery, diets or drugs must be initiated early in the pre-stroke patient. Towards this goal, two-dimensional linear B-scanning ultrasonography was explored, to visualize normal and abnormal extracranial vessels and to evaluate the longterm success of reconstructive vascular surgery.

PRINCIPLE

In this study, the principles, equipment and technique of ultrasound scanning are those developed for flaw detection in metal and for sonar and radar equipment.[1,2,6,19–22,24,26] Ultrasonic waves are generated by a pulse applied to a 3/4 inch barium titanate crystal at a fixed rate of 2,000 times/sec. When ultrasonic waves are directed into tissue, echoes return to the crystal face from tissue interfaces of different density or acoustic impedance. The same crystal, acting as a two-way energy converter by piezoelectric effect, receives reflected echo waves and converts them into electrical pulses, to be amplified and displayed as spots on an intensity modulated memory oscilloscope. A two-dimensional anatomic section, pictured on the oscilloscope, results from exact localization of the transducer in space, in both X-Y coordinates and angulation, by three 0.15 per cent conformity digital computer potentiometers. The equipment* used is illustrated in Figure 1.

METHOD

In contact ultrasonic B-scanning of extracranial vessels, the patient is placed in the supine position with the head elevated 15°. The neck is coated with mineral oil to provide acoustic coupling between transducer and skin. The transducer is then

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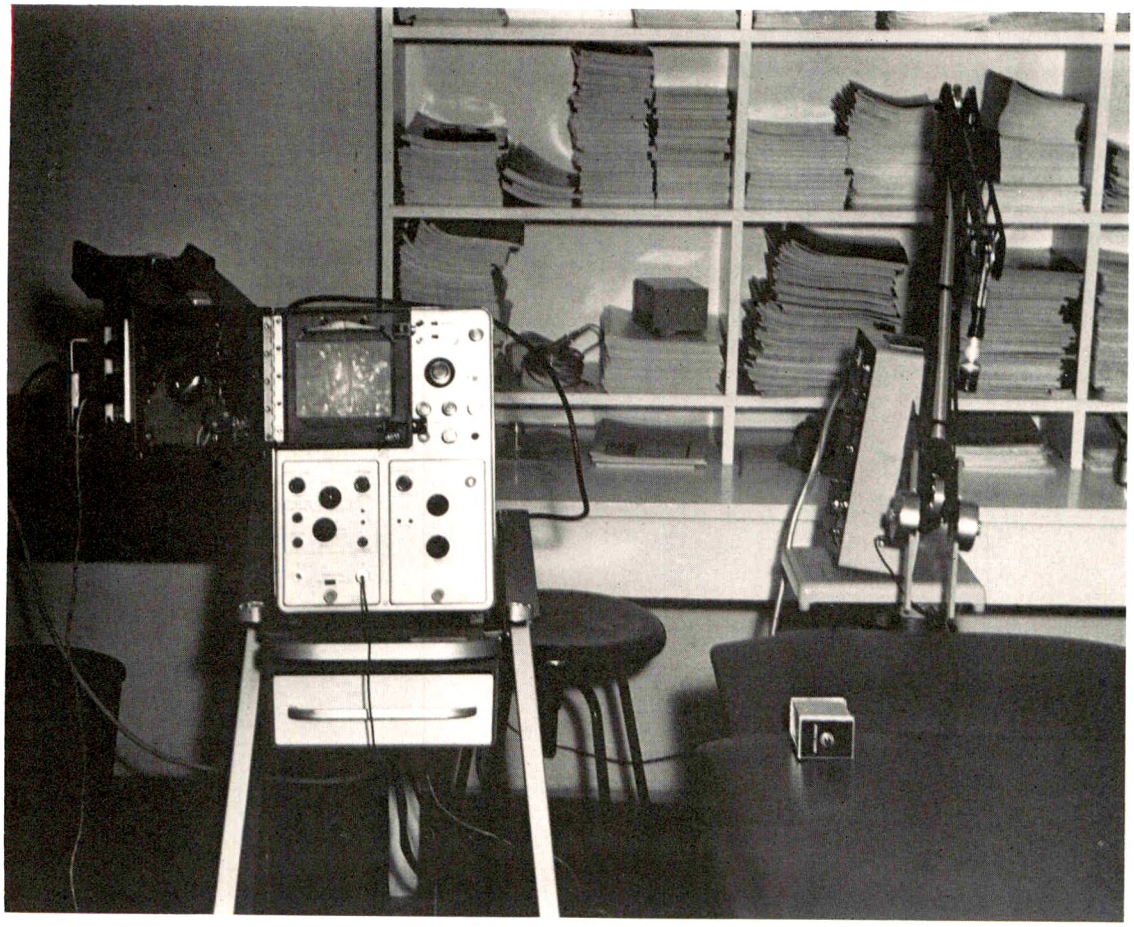


Fig. 1. Contact B-scan ultrasonographic equipment.

placed above the clavicle, medial to the sternocleidomastoid muscle, and moved approximately 3 cm./sec., by hand, with light pressure to avoid compression of the artery or possible embolization,[29] in a direct line from the proximal to the distal end of the carotid artery. The transducer is kept perpendicular to the longitudinal axis of the carotid artery throughout the scan to take advantage of the axial, or depth, resolution of the sound beam.[22,24] The oscilloscope screen is placed in such a position that the examiner can watch the scanning image or change the gain setting.[26] Serial longitudinal scans are made at precisely 3 mm. intervals to provide a composite picture[2] and aid in the localization of the carotid bifurcation. Once the carotid bifurcation is located, the examiner concentrates his efforts in this area, using vertical, horizontal, oblique and transverse scans with a variety of scanning methods, such as linear sector scanning, sector scanning or linear scanning.[22] The echosonogram is photographed by a Polaroid camera for permanent record. Because patients early in the study noted transient lightheadedness after prolonged scanning, subsequent patients were scanned for 5 minutes and allowed to sit up for 3 minutes. After each scan, the patient is queried for symptoms of cerebral vascular insufficiency.

MATERIAL

To evaluate ultrasonic visualization of arterial disease, 60 patients with known extracranial vascular disease, demonstrated by previous four-vessel angiography, were

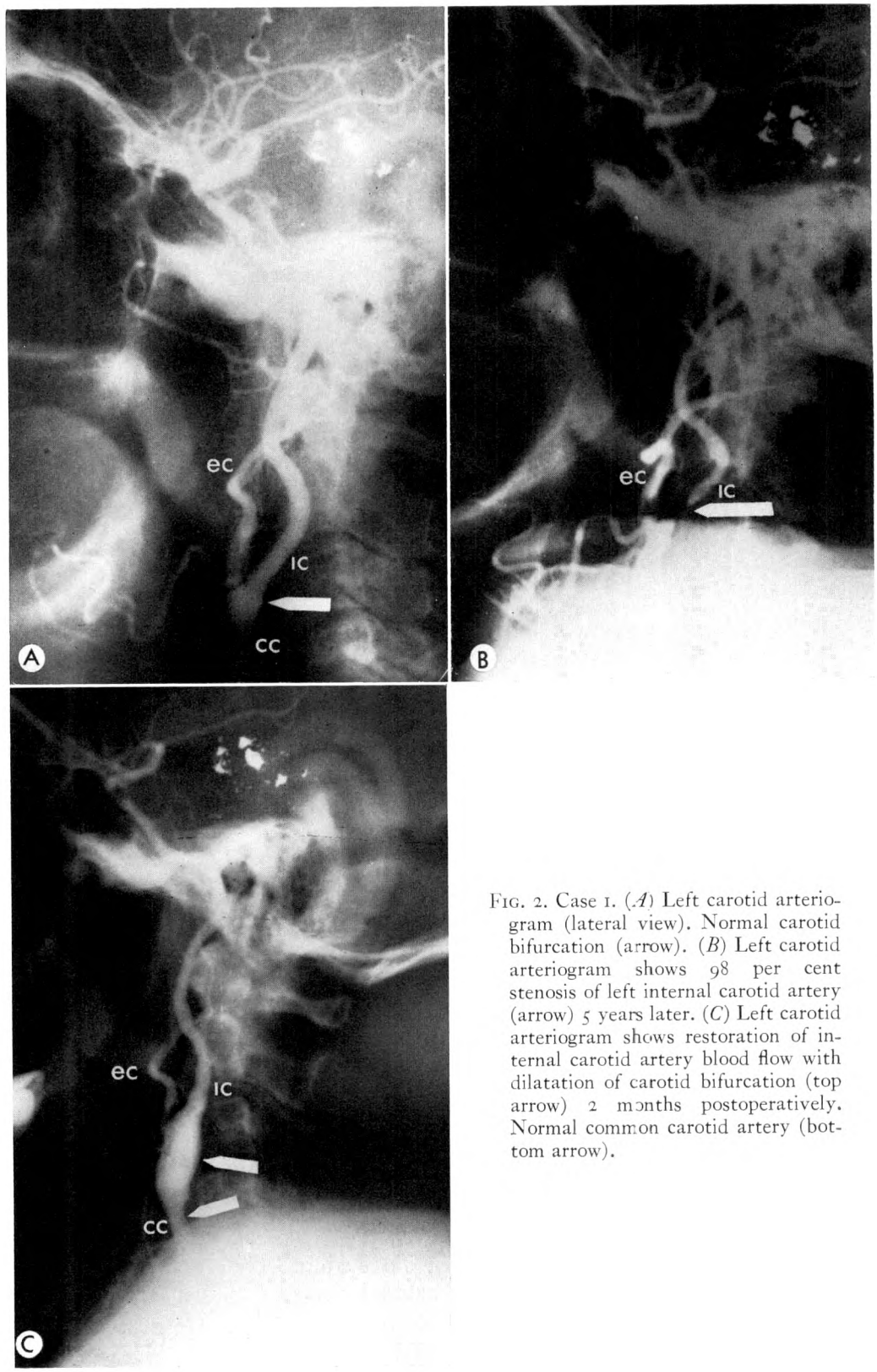


FIG. 2. Case 1. (*A*) Left carotid arteriogram (lateral view). Normal carotid bifurcation (arrow). (*B*) Left carotid arteriogram shows 98 per cent stenosis of left internal carotid artery (arrow) 5 years later. (*C*) Left carotid arteriogram shows restoration of internal carotid artery blood flow with dilatation of carotid bifurcation (top arrow) 2 months postoperatively. Normal common carotid artery (bottom arrow).

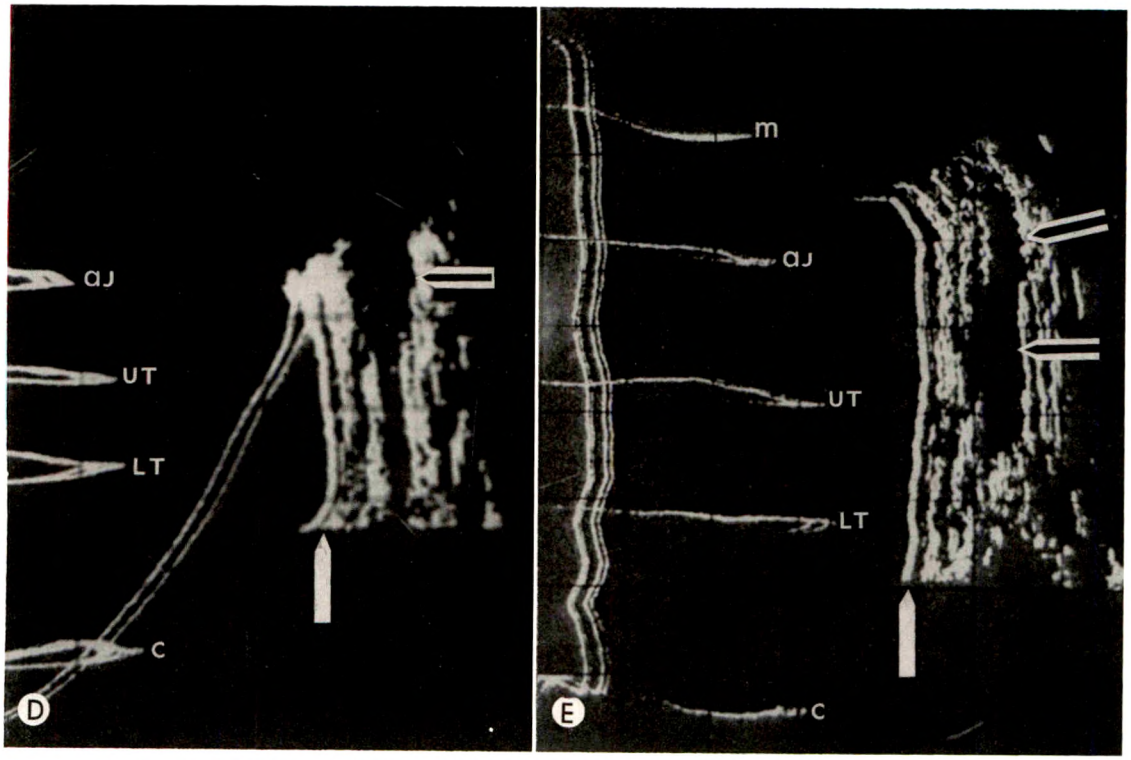


Fig. 2. (*D*) Left carotid echoarteriogram shows restoration of blood flow with dilatation of carotid artery (horizontal arrow) 2 months postoperatively. (*E*) Left carotid echoarteriogram shows a normal left internal carotid artery (top arrow) and carotid bifurcation (bottom arrow) 8 months postoperatively.

Note: On carotid echoarteriograms vertical arrows indicate direction of scanning and transducer-skin-line. EC—indicates external carotid artery, IC—internal carotid artery, CC—common carotid artery, V—vertebral artery, M—mastoid process, AJ—angle of the jaw, UT—upper border of the thyroid cartilage, LT—lower border of the thyroid cartilage, and C—clavicle. Calibration is 2 cm./1 cm. Echosonogram: 4×magnification.

selected for ultrasonic echoarteriography. The clinical histories emphasize the importance of early detection of vascular disease by a safe, nontraumatic screening method.

REPORT OF CASES

Case 1. A 77 year old man with increasing dizziness, unsteadiness in gait for 8 years, trouble with memory, and recent transient blindness in the left eye, showed a normal left carotid arteriogram in 1961 (Fig. 2*A*), and 98 per cent occlusion of the left internal carotid artery in 1966 (Fig. 2*B*). In this patient, as other investigators have noted, the progression of cerebrovascular symptoms with the advance of atherosclerosis,[5,15] suggested the need for a serial screening method. Normal blood flow was restored by endarterectomy surgery with a dacron prosthesis (Fig. 2*C*). Serial left carotid echoarteriograms substantiated patency of the carotid artery at 2 months and 8 months postoperatively (Fig. 2, *D* and *E*). The patient was alert and free of cerebrovascular symptoms 1 year later.

Comment: In 5 other patients, carotid echoarteriography was successful in demonstrating patency of the carotid bifurcation 2 months postendarterectomy with a dacron prosthesis (Fig. 3, *A–C*; and 10, *A* and *B*), supporting the potential use of B-scanning for the longterm evaluation of vascular surgery.

Case 11. In a 62 year old woman, a pulsating right supraclavicular mass, thought to be a carotid aneurysm, was shown to be a benign kinked common carotid artery by right brachial retrograde arteriography (Fig. 4*A*), and by right carotid echoarteriography (Fig. 4*B*).

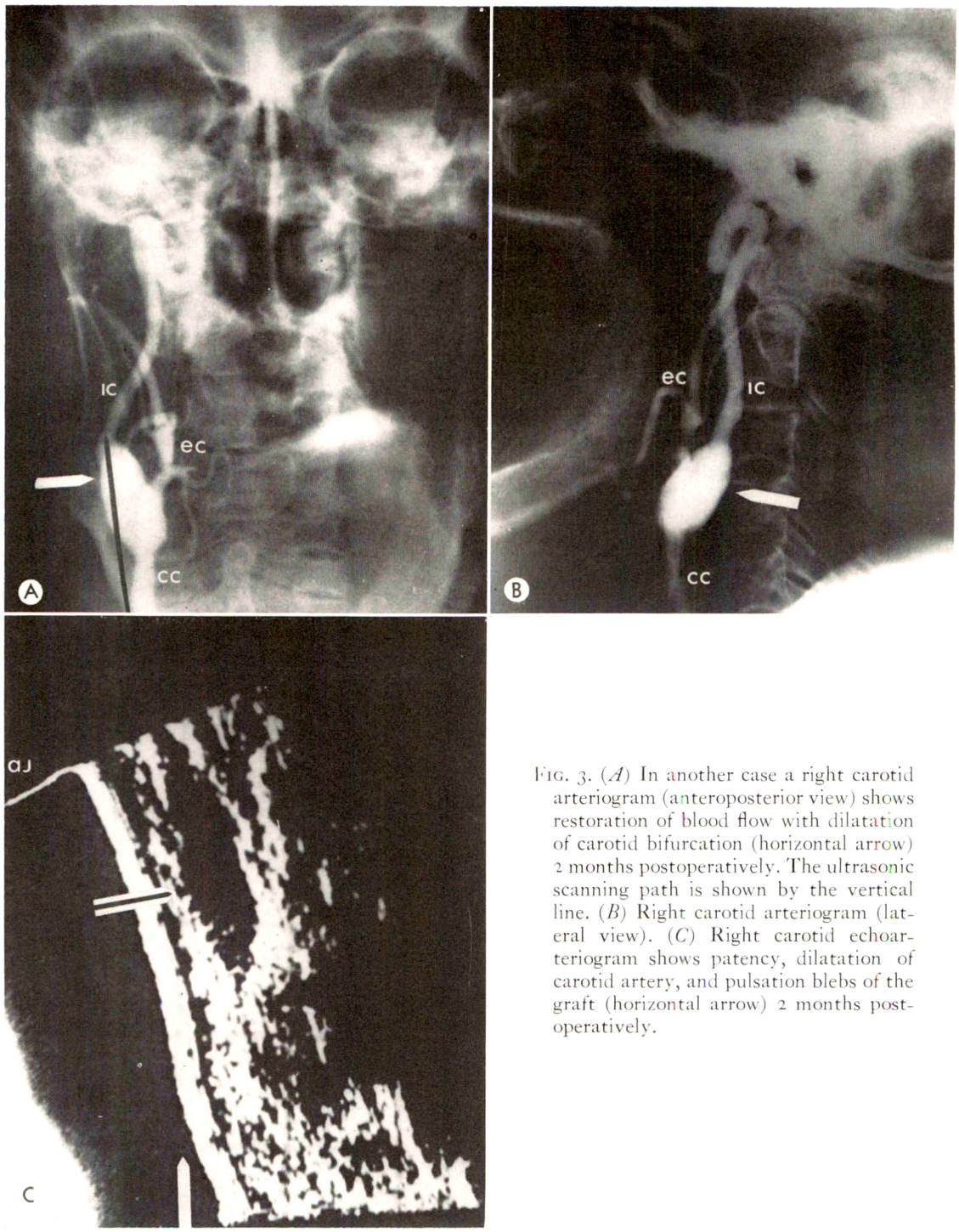


FIG. 3. (*A*) In another case a right carotid arteriogram (anteroposterior view) shows restoration of blood flow with dilatation of carotid bifurcation (horizontal arrow) 2 months postoperatively. The ultrasonic scanning path is shown by the vertical line. (*B*) Right carotid arteriogram (lateral view). (*C*) Right carotid echoarteriogram shows patency, dilatation of carotid artery, and pulsation blebs of the graft (horizontal arrow) 2 months postoperatively.

Comment: Kinked common carotid arteries were visualized by carotid echoarteriography in 7 other patients. The echosonogram shown in Figure 4*C* illustrates another case. Ultrasonic B-scanning is suggested as an atraumatic method for differentiating kinked arteries from aneurysms.

CASE III. A 41 year old woman with transient left-sided weakness, dizziness and blurring of vision when turning the head to the

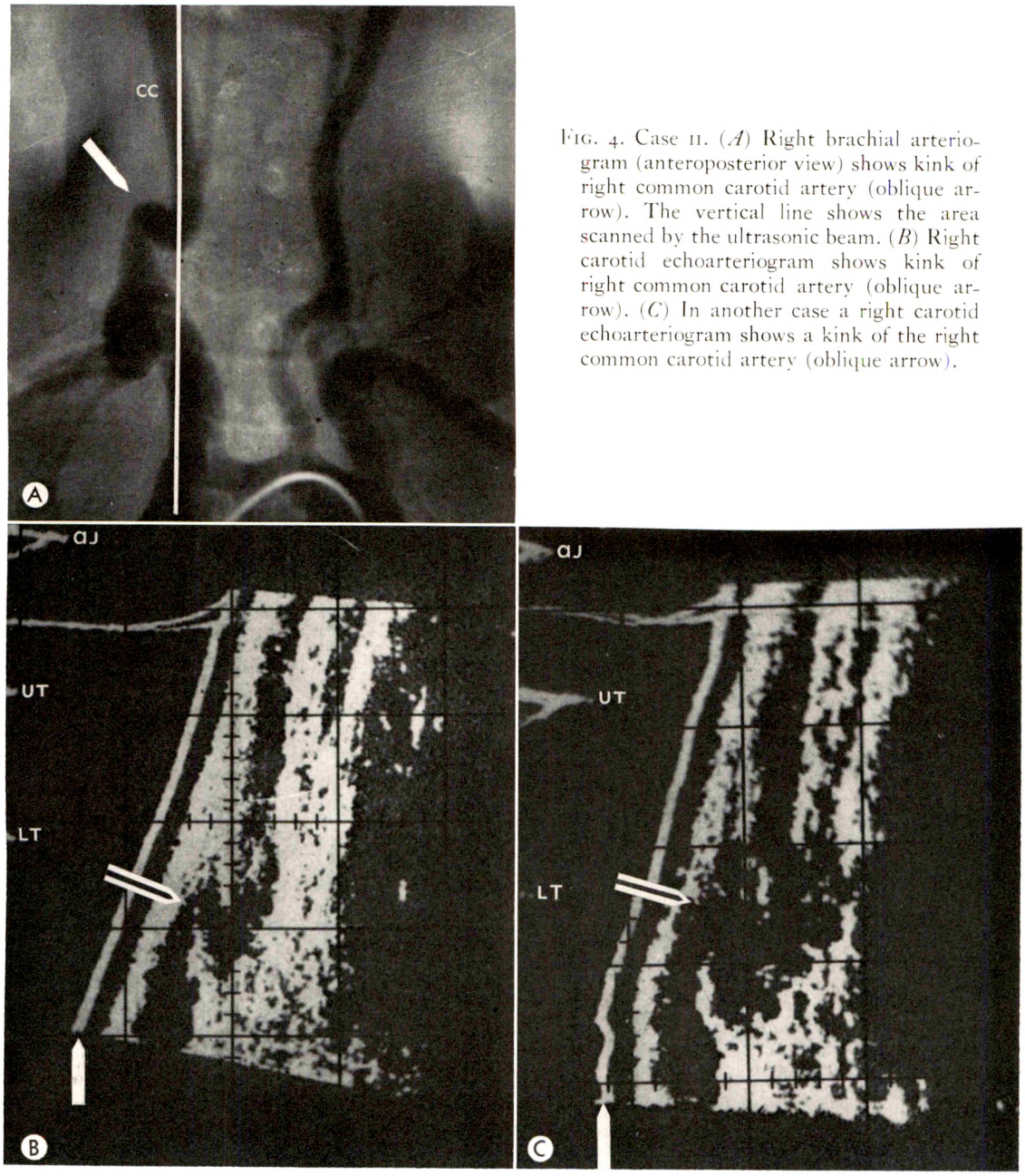


Fig. 4. Case II. (*A*) Right brachial arteriogram (anteroposterior view) shows kink of right common carotid artery (oblique arrow). The vertical line shows the area scanned by the ultrasonic beam. (*B*) Right carotid echoarteriogram shows kink of right common carotid artery (oblique arrow). (*C*) In another case a right carotid echoarteriogram shows a kink of the right common carotid artery (oblique arrow).

left, demonstrated a normal vertebral artery with a slight kink as it entered the vertebral foramen by right brachial arteriography (Fig. 5*A*). The echosonogram suggested a normal segment of the vertebral artery (Fig. 5*B*). Pulsation of the vertebral artery wall was noted on the oscilloscope screen but was not seen on the enlarged echosonogram.

Comment: A similar pattern has been noted in other patients. Ultrasonic scanning of the proximal vertebral artery should be possible and is under investigation in our laboratory. Kristensen[25] recently reported success in detection of normal carotid and vertebral arteries with a pulse-echo technique. In the future, ultrasonic B-scanning might spare such patients four-vessel angiography who lack a surgical lesion.

Case IV. A 40 year old man with "little strokes" for 6 years, with recent incomplete

recovery, showed 80 per cent stenosis of the left internal carotid artery on a left carotid arteriogram (Fig. 6*A*). Left carotid echoarteriography similarly suggested stenosis (Fig. 6*B*). A carotid bruit was located at the exact site of narrowing and aided in the analysis of the echosonogram.

Comment: In 3 other patients with internal carotid stenosis, similar echosonograms had been obtained. Eventually, ultrasonic B-scanning might visualize the development of atherosclerosis and permit objective measurement of the efficacy of diets or drugs in preventing or reversing the process.

CASE V. A 40 year old man with a 3 week history of headaches, transient left-sided weakness and sudden loss of speech on admission, with no improvement 1 year later, showed occlusion of the left internal carotid artery on left carotid arteriography (Fig. 7, *A* and *B*), and on left carotid echoarteriography (Fig. 7*C*).

Comment: A screening system, such as ultrasonic B-scanning, might have detected internal carotid stenosis in this patient before any symptoms of cerebrovascular insufficiency occurred, or at least during the headache period, suggesting possible contrast arteriography at a time before total occlusion. This, in turn, might have allowed early surgical or medical treatment before the permanent loss of speech in this young man.

CASE VI. A 44 year old man with infrequent episodes of blurring of vision, diplopia, dysarthria, and unsteadiness in gait for 4 years (recently severe enough to prevent his working), demonstrated total occlusion of all 4 major vessels on arteriography. Of interest, lipid, blood sugar, and coagulation studies were normal in this patient. The left carotid arteriogram and echoarteriogram are shown (Fig. 8, *A* and *B*). The echosonogram suggested occlusion of the left internal carotid artery.

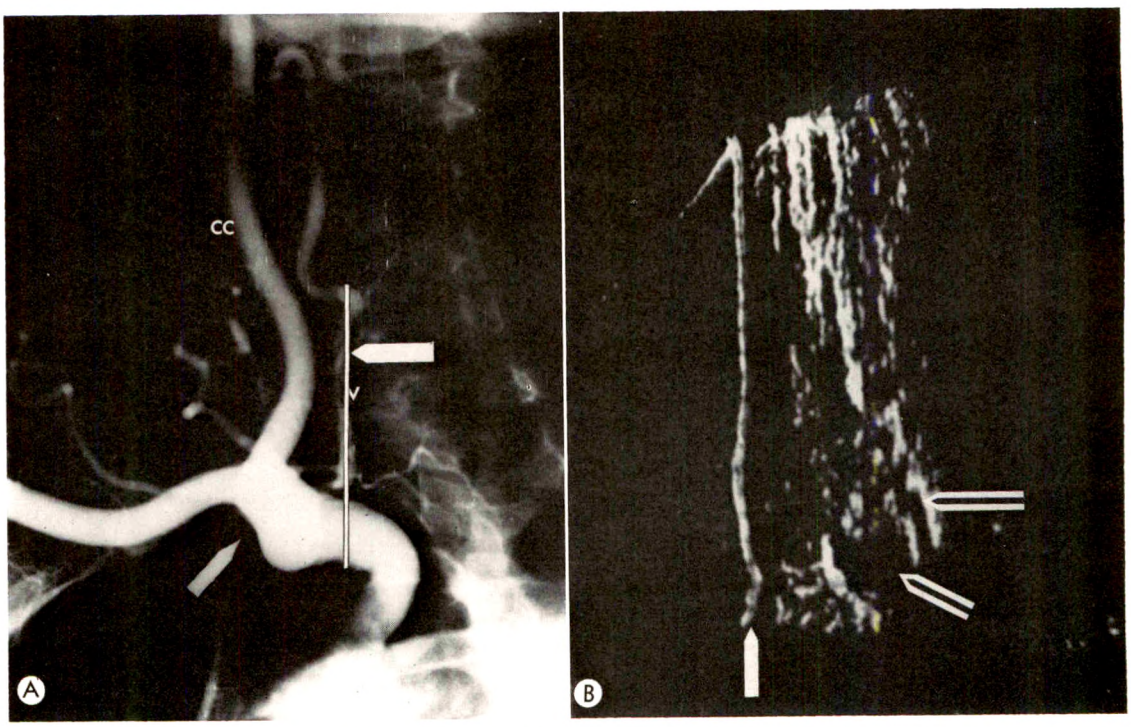


FIG. 5. Case III. (*A*) Right brachial arteriogram (anteroposterior view) shows vertebral artery (horizontal arrow) and innominate artery (oblique arrow). The vertical line shows the area scanned by the ultrasonic beam. (Right shoulder was elevated 45° with the head straight.) (*B*) Right echoarteriogram suggests vertebral artery (horizontal arrow) and innominate artery with pulsations in the posterior wall (oblique arrow). (Right shoulder was level, head straight and elevated 15°.) The vertebral artery is foreshortened with the right shoulder level and with the head elevated 15°. Anatomic positions must be taken into account when comparing contrast arteriograms and echoarteriograms.

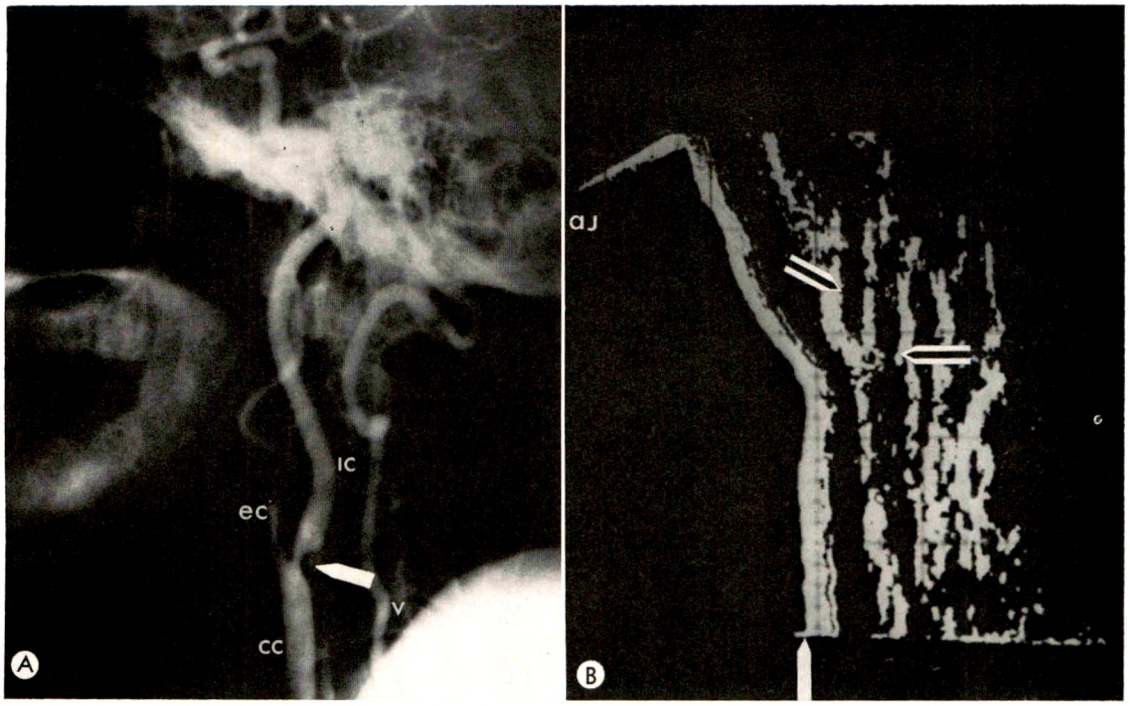


Fig. 6. Case IV. (*A*) Left carotid arteriogram shows 80 per cent stenosis of left internal carotid artery (oblique arrow). (*B*) Left carotid echoarteriogram shows 80 per cent stenosis of left internal carotid artery (horizontal arrow). External carotid artery appears large (oblique arrow), possibly due to parallel vessels or scanning artifacts.

Comment: In 5 other patients, internal carotid artery occlusions demonstrated by arteriography showed a similar carotid echoarteriographic pattern. The accuracy of ultrasonic B-scanning of internal carotid stenosis and occlusion, and the size of plaques detectable are under investigation. Here again, a pre-screening system might permit successful vascular surgery before occlusion of the arteries[4,5,13,27] and provide investigators with a procedure for studying the sequential development of atherosclerosis.

EXPERIMENTAL SUPPORT

To test the ability of ultrasonic B-scanning in visualizing the carotid artery, a carotid artery specimen which had been obtained from the postmortem room was suspended in a water-filled plastic container and scanned. Figure 9, *A* and *B* compares the removed carotid artery specimen with its echosonogram. Ultrasonic B-scanning was also performed immediately after death on 2 patients, and on 10 other patients in the postmortem room, with careful dissection and measurements to determine the relationship of echo patterns with the anatomic structures.

Two dogs, weighing 80 kg. or more, had neck scans, while chest thoracotomy permitted passage of guide wires and catheters from the aortic arch up to the bifurcation of the carotid artery to aid in the recognition of anatomic structures. Carotid echoarteriographic scanning was then done on patients during routine contrast carotid arteriography (Fig. 10*A*) while needles, guide wires and catheters were in place, to gain proof and orientation on echographic anatomy. In Figure 10*B* the carotid echoarteriogram shows a guide wire in the common carotid artery of a patient 2 months postendarterectomy surgery, and a dacron prosthesis.

The common carotid artery was also identified by a B-mode display method, (Fig. 10*B*, insert). B-mode is an intensity

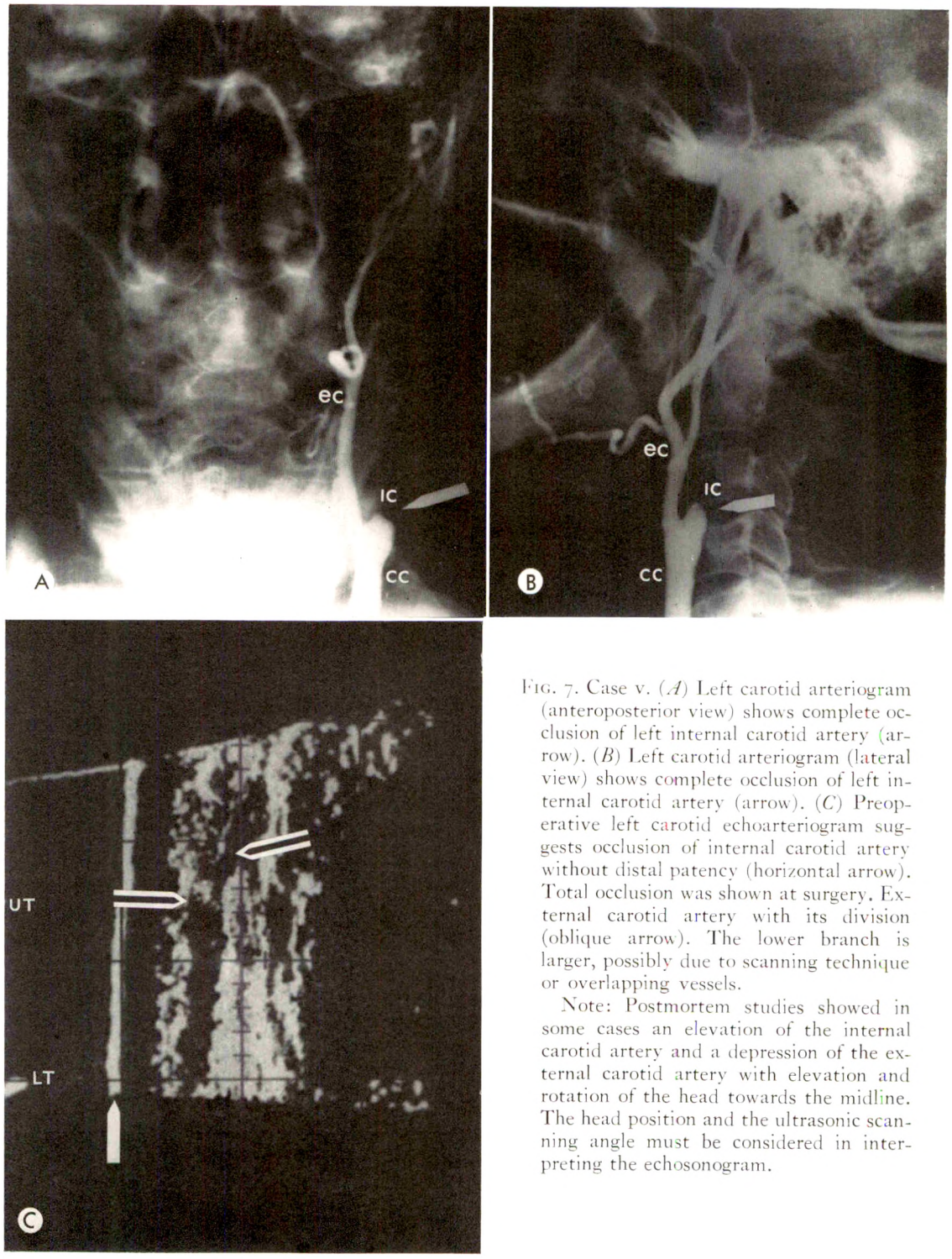


FIG. 7. Case v. (*A*) Left carotid arteriogram (anteroposterior view) shows complete occlusion of left internal carotid artery (arrow). (*B*) Left carotid arteriogram (lateral view) shows complete occlusion of left internal carotid artery (arrow). (*C*) Preoperative left carotid echoarteriogram suggests occlusion of internal carotid artery without distal patency (horizontal arrow). Total occlusion was shown at surgery. External carotid artery with its division (oblique arrow). The lower branch is larger, possibly due to scanning technique or overlapping vessels.

Note: Postmortem studies showed in some cases an elevation of the internal carotid artery and a depression of the external carotid artery with elevation and rotation of the head towards the midline. The head position and the ultrasonic scanning angle must be considered in interpreting the echosonogram.

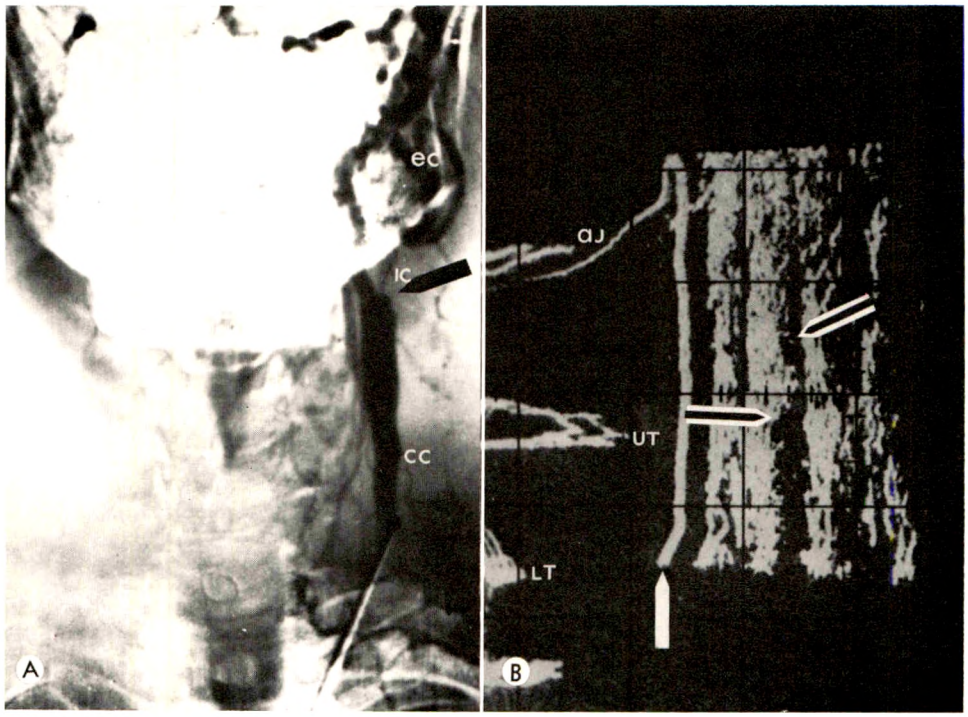


Fig. 8. Case VI. (*A*) Left carotid arteriogram (anteroposterior view) shows internal carotid artery occlusion (arrow). (*B*) Left carotid echoarteriogram shows internal carotid artery occlusion (horizontal arrow) and external carotid artery (oblique arrow).

modulated presentation of echoes shown as dots on the oscilloscope screen. By virtue of a moving time base, the artery wall pulsation is generally shown moving in an opposite direction.[10,14,18,19,25,30] With this method the transducer is maintained in a fixed position.

The identification of an artery is also possible by stopping the transducer and holding it stationary during a carotid echoarteriographic scan, while the horizontal shift control of the cathode-ray screen is slowly moved to trace the pulsating artery. Donald and Brown,[6] in 1961, used this method to outline an abdominal aortic aneurysm.

In interpreting a carotid echoarteriogram, the echosonogram was enlarged to life-size and compared to the carotid arteriogram with corrections for x-ray magnification. The cross-sectional anatomy drawings of the neck by Eycleshymer and Schoemaker[11] and the excellent echosonographic cross-sectional anatomy pictures of the neck by Howry,[21] were enlarged to life-size and placed beside the echosonogram and carotid arteriogram pictures under study. A stereographic atlas of the human neck was used as well. The mastoid process, the angle of the jaw, upper and lower border of the thyroid cartilage and clavicle were marked on carotid echoarteriographic scans, and compared to identical structures on contrast carotid arteriograms by measurements, facilitating recognition of lesions and echo patterns. The site of a bruit was marked on the echosonogram as an additional aid. Of further value in recognizing echographic structures was the ultrasonic B-scanning of unusual clinical cases, such as a kinked common carotid artery, a previously endarterectomized artery with a dacron prosthesis, and an aneurysmal dilatation of the carotid bifurcation (Fig. 11, *A* and *B*). In patients undergoing vascular surgery, the echosonogram and

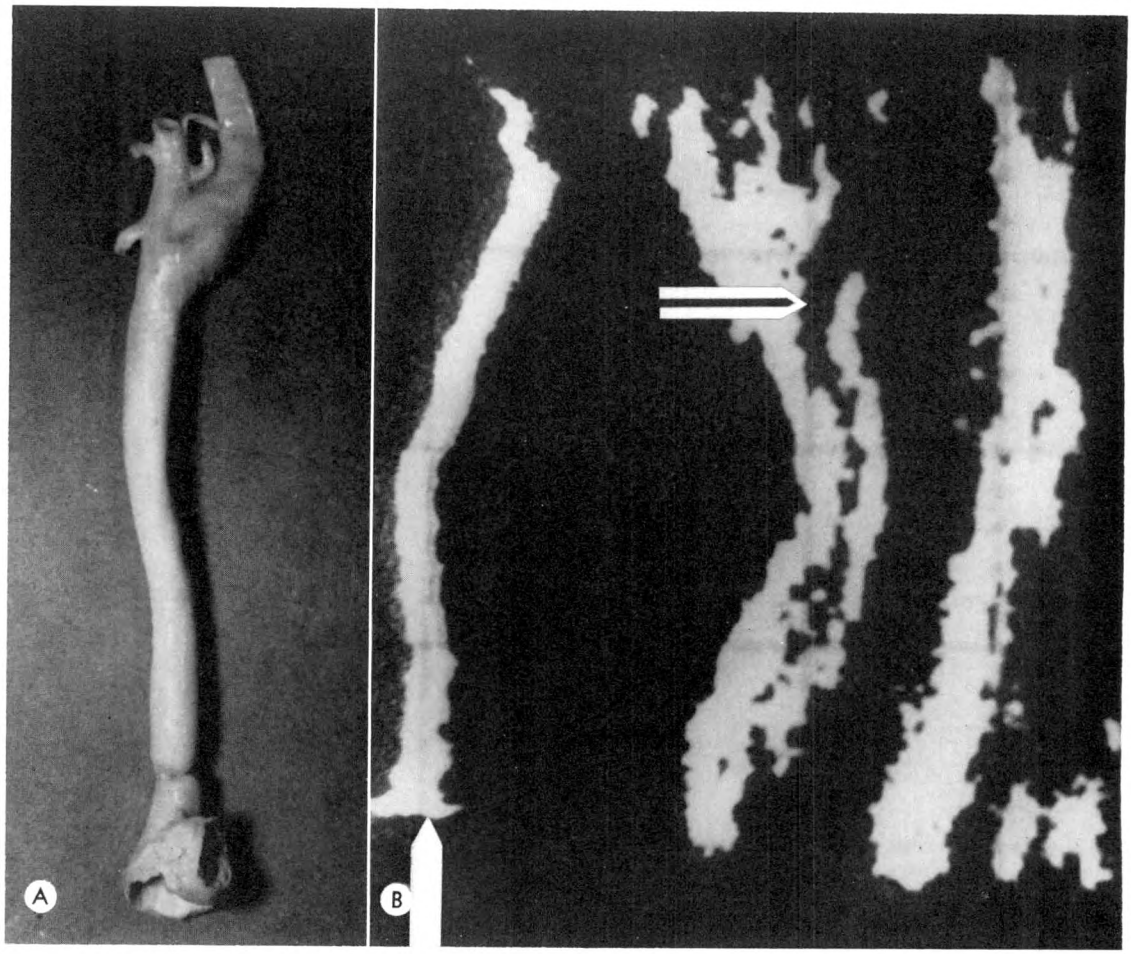


FIG. 9. (*A*) Gross specimen of the carotid artery with adventitia removed. (*B*) Carotid echoarteriogram shows an echoless lumen with echo reflections of the adventitia. Superior thyroid artery (horizontal arrow). Specimen was suspended in a plastic water-filled container and scanned.

arteriogram were brought to the operating room to identify muscles, veins, and arteries seen on the echographic scans.

Some problems in interpreting carotid echosonograms were due to the overlapping of vessels, to the lack of standardization of the equipment and techniques of scanning, and to the lack of experience in adjusting the equipment for differences in body build and muscular tension.[1,2,20,26] Interpretation was also hampered by the lack of anatomic drawings of the neck in the longitudinal plane. Once the examiner learns to recognize the relationship of anatomic structures to the carotid artery, the interpretation of the carotid echosonogram is made easier. Serial longitudinal and cross-sectional scans were essential in recognizing artifacts and establishing whether the vessel was normal or abnormal.

HISTORICAL SUPPORT

To further substantiate the ability of ultrasound to visualize normal and abnormal vessels, a brief review of the use of ultrasound to visualize the circulatory system is given. In 1950, Keidel[23] demonstrated ventricular contractions by a continuous-transmission ultrasonic method. In 1954, Edler and Hertz,[9] and Edler,[8] in 1955, reported that pulsed ultrasound, using A-mode method, could localize the interfaces between the heart wall and its blood filled cavities, measure the thickness of the heart

wall, detect thrombi in heart chambers, and localize the interfaces between the vessel walls and their fluid contents in an isolated calf's heart preparation. Soon, they showed the presence of mitral valvular disease, intra-auricular thrombi, changes in the outflow tract of the ventricle, and pericardial effusion in living subjects. Wild, Crawford and Reid,[32] in 1957, using a B-scanning method, demonstrated the coronary artery, the aorta, and a myocardial infarction in a freshly excised postmortem heart. In 1965, Hertz and Olofsson,[17] and Hertz,[16] in 1967, reported the use of an ultrasonic mirror system to outline the cross-sectional anatomy of the heart. Ebina *et al.*,[7] in 1967, reported the use of ultrasonotomography to visualize the heart and great vessels in living subjects. In 1961, Donald and Brown[6] showed an abdominal aortic aneurysm using ultrasound. Segal *et al.*,[30] in 1966, demonstrated the size of the lumen and the presence of intramural thrombus in an abdominal aortic aneurysm using A and B-mode methods. Goldberg and coworkers[14] in 1966, using A-mode, B-mode and B-scan determined the thickness of the aortic wall, outlined aortic aneurysms and their lumen size. Evans *et al.*[10] reported similar results in 1967. Ultrasonic observation of peripheral arteries was reported by

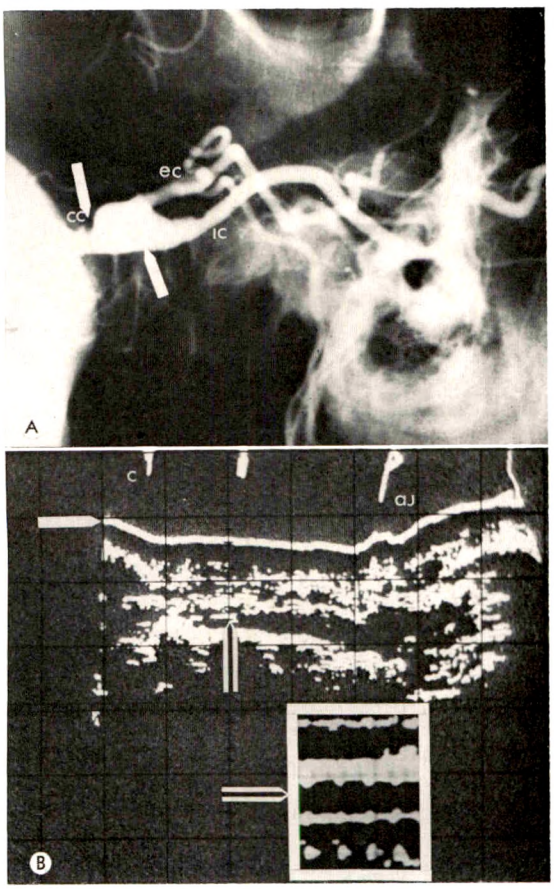


Fig. 10. (*A*) Left lateral carotid arteriogram (viewed horizontally) shows patency and dilatation of carotid bifurcation (bottom arrow) 2 months postoperatively. Normal common carotid artery (top arrow). (*B*) Left carotid echoarteriogram (viewed horizontally) shows patency and dilatation of the carotid artery bifurcation 2 months postoperatively. A guide wire shows as an interrupted white line within the common carotid artery (vertical arrow). Insert shows the common carotid artery and its pulsations by B-mode display (black horizontal arrow).

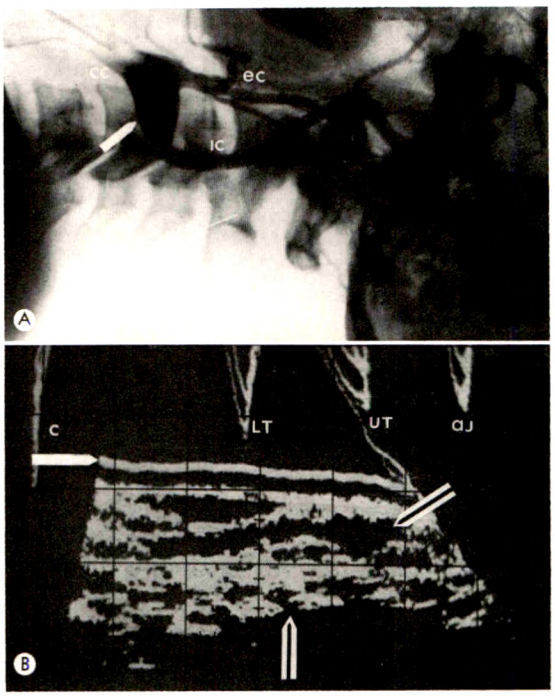


Fig. 11. (*A*) Left lateral carotid arteriogram (viewed horizontally) shows aneurysmal dilatation of the carotid bifurcation (oblique arrow). (*B*) Left carotid echoarteriogram (viewed horizontally) shows aneurysmal dilatation of carotid bifurcation (oblique arrow). Note convexity of common carotid artery prior to its bifurcation. Cervical transverse process (vertical arrow).

Masterson, Keeler and Silver,[28] in 1966, and Holm and Kristensen,[18] in 1967. In 1954, Holmes and associates,[19] using a compound ultrasonic scanning method, showed cross-sectional pictures of the carotid artery, internal jugular vein and muscle masses. A cross-section of a carotid bifurcation aneurysm was reported by Howry and Gordon,[22] in 1964. In 1967, Kristensen[25] reported an ultrasonic pulse detection method to show normal carotid and vertebral arteries. Von Wowern and Hansen[31] reported, that same year, detection of carotid artery disease using the same method.

CONCLUSION

Because blood lacks echo-reflective interfaces, extracranial arteries would appear ideally suited for visualization of an echo-producing plaque or thrombus which extends into the lumen of the artery. The ultrasonic scanning of the carotid bifurcation is aided further by its closeness to the skin surface and by the lack of overlying air-filled structures which block ultrasound transmission. The echoless black carotid arteriogram, although relatively crude in this developmental stage in comparison to the roentgenographic arteriogram, could provide useful information to the physician and be of increasing value as a diagnostic aid as more investigators enter the field and as equipment and scanning techniques are improved. Since vascular surgery carries a high mortality and morbidity rate in acute and progressive strokes, in contradistinction to the effectiveness and safety of surgery in transient ischemic attacks or so-called "little strokes," the early detection of extracranial vascular disease by a simple and safe method prior to a stroke is of paramount importance.

SUMMARY

A safe and simple ultrasonic contact carotid echoarteriographic B-scanning method is described. The potential use of ultrasonic B-scanning for detection of extracranial occlusive disease before a stroke, and for longterm evaluation of atherosclerosis and its treatment, is suggested by comparing the results of the ultrasonic echoarteriogram with its analogue, the roentgenographic arteriogram, in patients with kinked common carotid artery, internal carotid artery occlusion and stenosis, normal vertebral artery, and in determining patency of internal carotid artery previously subjected to vascular surgery.

Experimental dog and postmortem ultrasonic scanning studies and a historical review of the use of ultrasound to visualize the circulatory system are given in support of this work and to encourage other investigators into this field.

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THE PONTINE ARTERIES IN VERTEBRAL ANGIOGRAPHY*

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THE pontine arteries have, in the past, been well demonstrated on roentgenograms of anatomic specimens[3,4,7] (Fig. 1). We are not aware of any previous attempt to study these arteries systematically during life. The present work is such an attempt to investigate the appearance and frequency of visualization of the pontine arteries by vertebral angiography.

ANATOMY

Although the anterior inferior and superior cerebellar arteries are important sources of blood supply to the pons, only the pontine branches of the basilar artery will be described here. According to Stopford,[9] there are a median and a transverse set of pontine branches of the basilar artery.

The median branches are numerous, minute twigs which quickly enter the anterior part of the pons along the median groove. These tiny arteries are apparently referred to by Hassler[3] as the paramedian arteries, by Kaplan and Ford[4] as medial perforators, and by Krayenbühl and Yaşargil[5,6] as median and paramedian pontine arteries.

The transverse rami of the basilar artery are generally symmetric, variable in size and number, but larger and less numerous than the median set.[9] They originate bilaterally from the posterolateral aspects of the basilar artery and are closely related to the anterior and anterolateral borders of the pons, giving off perforating branches along their path and finally entering the brain completely. These are probably the pontine arteries which Kaplan and Ford[4] call the lateral perforators. They state that there are generally 4 to 6 pairs of pontine perforators. The transverse rami seem to be called the circumferential branches by Hassler[3] and the short circumferential or short circumflex pontine arteries by Krayenbühl and Yaşargil.[5,6]

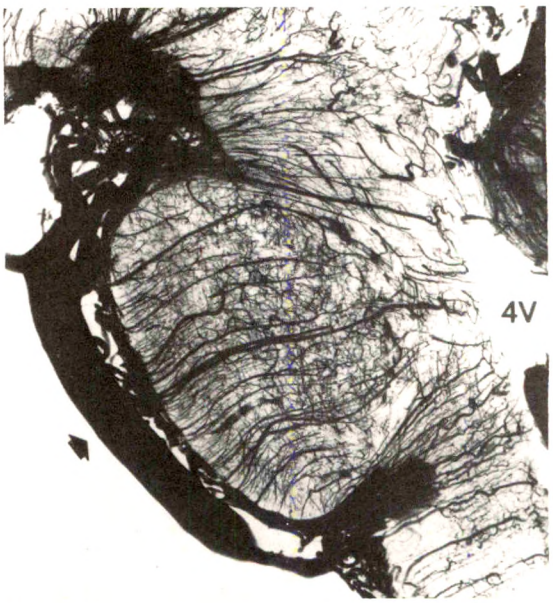


FIG. 1. Microangiogram of anatomic specimen in the lateral projection showing the numerous branches of the basilar artery supplying the pons. The basilar artery (arrow) and the fourth ventricle (4V) are labeled. (Reproduced through the courtesy of G. Salamon and *Ann. Radiol.*[7])

MATERIAL

In another investigation of the pontomesencephalic veins, we reviewed the 1967–1968 vertebral angiographies performed at Ullevål Hospital.[1] We selected for further study the first 100 examinations encountered with a technically satisfactory demonstration of the posterior cranial fossa veins as demonstrated in the lateral projections. These 100 vertebral angiographies (8 right and 92 left) also served as the

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This investigation was accomplished in part during the period when one of the authors (T.O.G.) was the recipient of the Association of University Radiologists Travel Study Award for 1968.

Table I

AGE DISTRIBUTION OF PATIENTS

Age (yr.)	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79
No. of Patients*	9(9)	8(8)	12(11)	12(6)	20(8)	25(4)	11(0)	3(0)

* Of the total number of vertebral angiographies for each group, the number of selective vertebral angiographies is indicated in parentheses.

material for the current investigation of the pontine arteries.

Only 1 examination per patient was included. Thirty-seven patients were males and 63 were females. Their ages ranged from 5 months to 74 years (Table 1). Angiography was performed by catheterization from the femoral arteries in all cases. Most of the 46 selective vertebral angiographies had been done on patients less than 45 years old. The remaining 54 examinations were obtained by injecting 18–20 ml. contrast material (280 mg. iodine per ml.) into the left subclavian artery just proximal to the origin of the vertebral artery.

Of those patients who had fairly good visualization of both the pontine arteries and pontomesencephalic veins in the lateral projection, 24 also had pneumoencephalography in which the brain stem was well outlined with generous amounts of gas, and laminagraphy by means of hypocycloidal motion (polytome). No patient in the entire series had a known posterior cranial fossa mass.

FINDINGS AND DISCUSSION

Tönnis and Schiefer[10] stated in 1959 that the arteries to the pons, the internal auditory artery, and the anterior inferior cerebellar artery have no significance angiographically because these small arteries cannot be seen with certainty through the dense bone structures in the lateral projection. Krayenbühl and Yaşargil[5,6] expressed the same opinion, adding in 1965 that these arteries are seldom seen even with stereoscopy; however, they did find subtraction helpful.

In the present material, we could identify at least some pontine arteries in 72 per cent of the vertebral angiographies in the lateral projection and 23 per cent in the anteroposterior projection. The incidence of visualization was 87 per cent in the lateral views and 41 per cent in the frontal views for selective vertebral angiographies, as compared to 59 per cent and 7 per cent on the lateral and frontal roentgenograms, respectively, in those examinations with an injection of contrast material into the left

Table II

RELATIVE DEGREE OF VISUALIZATION OF PONTINE ARTERIES BY VERTEBRAL ANGIOGRAPHY

	Vertebral Angiography (100 examinations)			
	Injection in Subclavian Artery (54 examinations)		Injection in Vertebral Artery (46 examinations)	
Opacification	Lateral view	Anteroposterior view	Lateral view	Anteroposterior view
Unsatisfactory	22	50	6	27
Fair	27	4	27	16
Good	4	0	10	3
Excellent	1	0	3	0
Cases with opacification	32(59%)	4(7%)	40(87%)	19(41%)

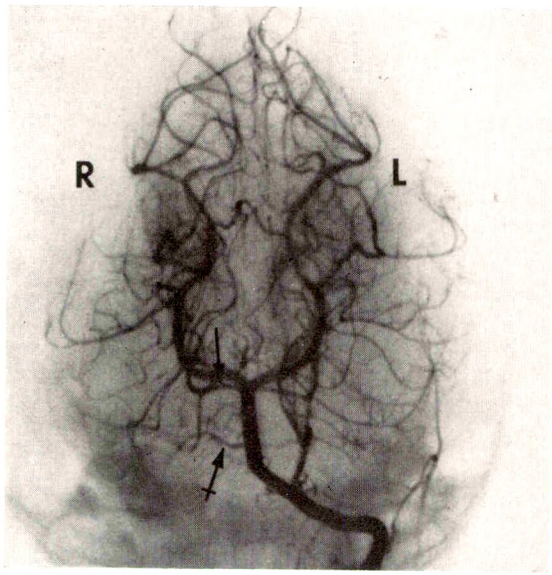


FIG. 2. Subtraction selective left vertebral angiogram in 5 month old boy. Pontine arteries are opacified better on the right than the left. They are projected between the right superior (arrow) and anterior inferior (crossed arrow) cerebellar arteries.

subclavian artery (Table II). Visualization was judged on the basis of the routine roentgenograms and not the subtraction studies.

Selective vertebral angiography appears to be important for visualization of these small arteries. In our experience, they are seldom seen in retrograde brachial angiography. Visualization of the tiny pontine arteries seems to be more dependent on selective vertebral angiography than is the case with a satisfactory demonstration of the posterior cranial fossa veins.[1] This is undoubtedly related to the degree of stoppage of blood flow from the opposite vertebral artery and the concentration of contrast material in the basilar artery, which may be more critical for satisfactory opacification of the small pontine arteries than veins of a larger caliber. The rate of blood flow in arteries *versus* veins may be another related factor.

We find subtraction studies very useful in evaluation of the pontine arteries, especially in the anteroposterior projection (Fig. 2). Subtraction is less helpful in the lateral views because the upper pontine arteries can often be seen almost equally well on the original roentgenograms. The

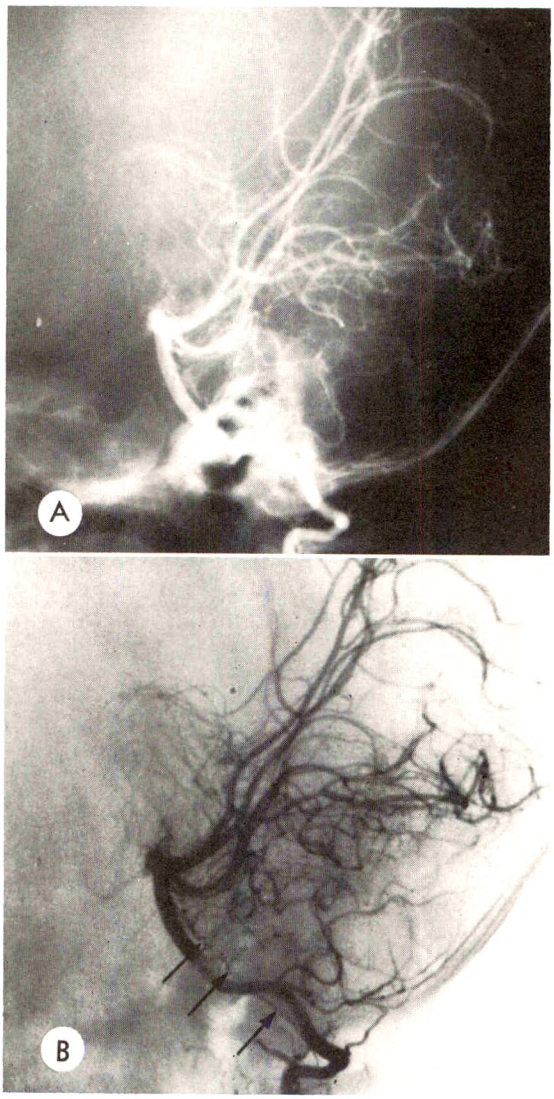


FIG. 3. (*A*) Lateral selective right vertebral angiogram in a 6 month old boy with cerebral aqueduct stenosis proven by pneumoencephalography and ventriculography. The origins of some of the pontine arteries can be seen as tiny strings of increased density through the posterior part of the basilar artery. (*B*) Subtraction study of *A*. Tiny arteries outlining the anterior part of the medulla oblongata and lower pons are now better demonstrated (arrows). The pontine arteries are usually seen best where they turn sharply immediately adjacent to the anterior border of the pons but in this examination can also be seen well anterior and posterior to this level.

more caudal pontine arteries usually cannot be seen even on subtraction films, since a generally satisfactory lateral exposure of a vertebral angiogram does not sufficiently penetrate the dense petrous bones. Exceptions to this are encountered mostly in young children (Fig. 3, *A* and *B*).

Westberg[11] and Hara and Fujino[2] have described the angiographic appearance of the perforating thalamoperforate arteries. The latter authors state that the cisternal and parenchymal portions of these arteries can be clearly distinguished from each other. We agree that these and other small arteries coursing along the roof of the interpeduncular fossa not infrequently seem to make a sharp turn as they enter the brain parenchyma (Fig. 4; and 6*A*). We also find the pontine arteries helpful in locating the anterior border of the pons, especially when the pontomesencephalic veins are faintly visualized.

In lateral vertebral angiograms, the origins of the pontine arteries can occasionally be seen as tiny areas of increased density of contrast material through the opacified basilar artery (Fig. 3*A*). The pontine arteries can more frequently be identified as they pass posteriorly, and occasionally are clearly shown to make a distinct turn one or two millimeters from their origins (Fig. 3, *A* and *B*). The location of this distinct alteration in course appears to be immediately adjacent to the anterior border of the pons and is generally where the pontine arteries are most easily demonstrated (Fig. 5*A*; and 6*A*). The pontine branches in this area are probably projected almost axially in the lateral roentgenograms. We believe that only the transverse or circumferential set of pontine arteries are ordinarily demonstrable by vertebral angiography.

The pontomesencephalic veins are very

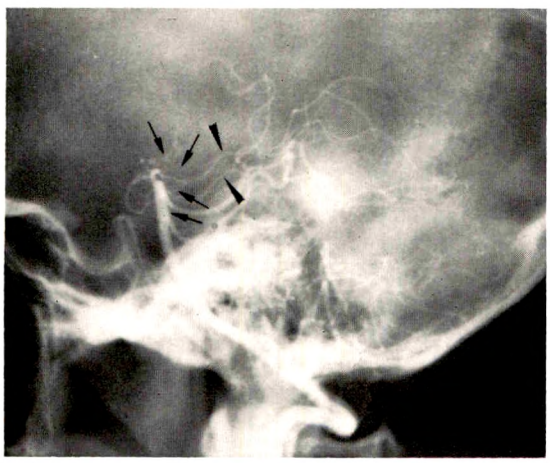


Fig. 4. Lateral selective left vertebral angiogram in a 21 year old woman. The pontine arteries and small arteries in the interpeduncular fossa delineate the anterior border of the brain stem (arrows). The posteromedial choroidal (arrowheads) and superior cerebellar arteries are also unusually well shown because the posterior cerebral arteries in this patient were opacified only by carotid angiography (not shown).

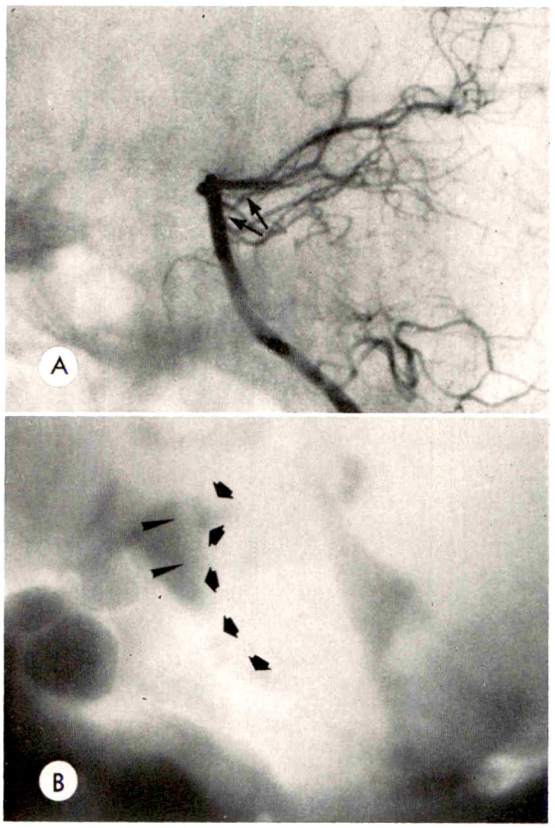


Fig. 5. (*A*) Subtraction, lateral selective left vertebral angiogram in a 26 year old woman. The pontine arteries (arrows) are visible only adjacent to the upper anterior border of the pons. (*B*) Pneumoencephalogram of the same patient as in *A*. Note the relationship of the basilar artery (arrowheads) to the brain stem (arrows).

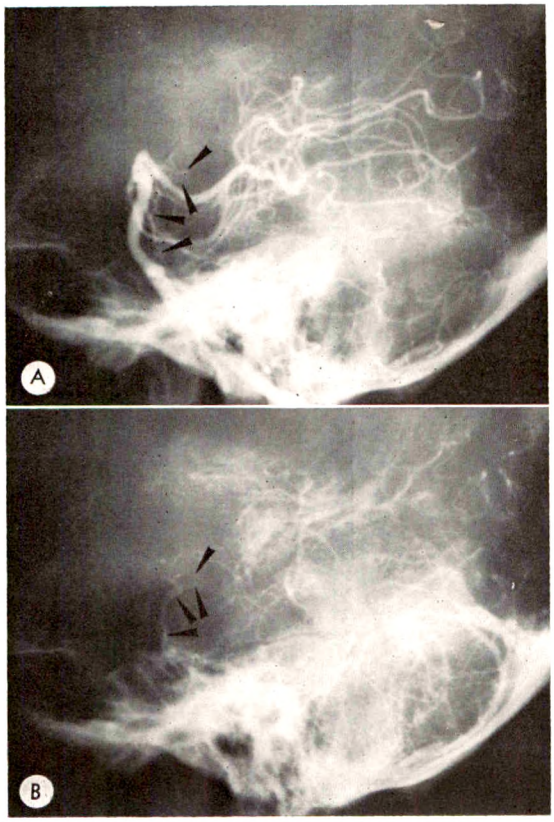


FIG. 6. (*A*) Lateral left vertebral angiogram by injection of contrast material into the left subclavian artery of a 51 year old woman. The basilar artery is tortuous. The anterior margin of the brain stem (arrowheads) is much more accurately indicated by the pontine arteries and the posterior thalamoperforate arteries. (*B*) Venous phase of same examination as in *A*. The pontomesencephalic veins (arrowheads) confirm the localization of the brain stem shown in *A*.

helpful in locating exactly the anterior, upper border of the brain stem[1] (Fig. 6*B*). These veins will often completely overlap the pontine arteries and may cancel out the

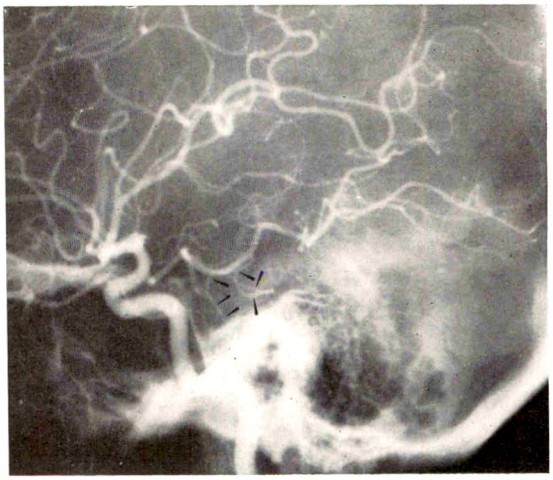


FIG. 7. Lateral left carotid angiogram of a 21 year old woman. Note prominent temporal branch (arrowheads) of left posterior cerebral artery. The pontine arteries are not visualized.

contrast material in the arteries if a lateral projection of the vertebral angiogram during the arterial phase is superimposed on the venous phase by means of subtraction.

In the current material, we thought that the pontine arteries could be identified well enough in the lateral projections of 54 examinations to aid in locating the anterior, upper margin of the pons. This represents a considerably smaller number of vertebral angiographies than those demonstrating the pontine arteries to at least some extent. Of these 54 cases, 51 had satisfactory visualization of the pontomesencephalic veins and 24 of the 51 had pneumoencephalography, in which the brain stem was well outlined with air. There was good correlation between the location of the anterior border of the pons as indicated by the pon-

TABLE III

CORRELATION BETWEEN PONTINE ARTERIES AND PONTOMESENCEPHALIC VEINS FOR LOCALIZATION OF UPPER, ANTERIOR BORDER OF BRAIN STEM

	Discrepancy (51 cases)				
	Veins in Front of Arteries		"None"	Veins Behind Arteries	
	2–3 mm.	1–2 mm.	0–1 mm.	1–2 mm.	2–3 mm.
No. of Cases	0	2(4%)	41(80%)	7(14%)	1(2%)

tomesencephalic veins and pneumoencephalography as compared to the pontine arteries (Table III; Fig. 5, *A* and *B*; and 6, *A* and *B*). However, the pontomesencephalic veins are more often clearly visualized than the pontine arteries and are consequently more helpful in locating the anterior border of the brain stem by angiography.[4]

Although the basilar artery is generally quite closely related to the anterior border of most of the brain stem, this is not always true, especially for the distal part of the basilar artery and, particularly, when the basilar artery is long and tortuous[8] (Fig. 5*A*; and 6*A*). However, it is in the upper pontine region that the pontomesencephalic veins and pontine arteries are most easily seen and would seem to be most useful in locating the anterior border of the brain stem angiographically (Fig. 4; 5*A*; and 6, *A* and *B*).

A temporal branch of the posterior cerebral artery in the lateral roentgenograms is sometimes projected near the anterior margin of the pons and could be mistaken for the pontine arteries (Fig. 7; and 8, *A* and *B*).

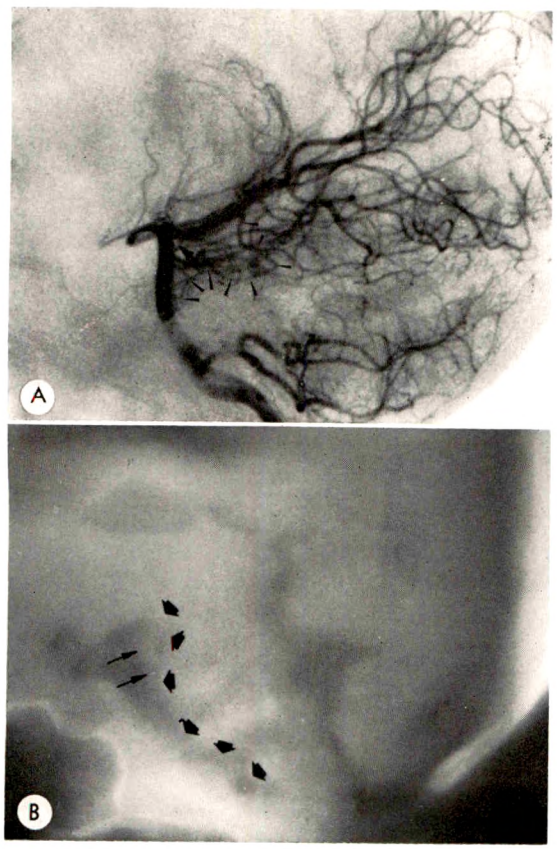


FIG. 8. (*A*) Subtraction, lateral selective right vertebral angiogram in a 24 year old woman. The pontine arteries (arrow) are difficult to see. Confusion could arise because part of a temporal branch (arrowheads) of one posterior cerebral artery is projected near the anterior border of the pons. Compare with Figure 7 and 8*B*. (*B*) Pneumoencephalogram of same patient as in *A*. Lateral laminagraphic section obtained in a slightly parasagittal location shows the relationship of the brain stem (short arrows) to the distal part of the basilar artery (long arrows). The basilar artery in this patient is in relatively close contact with even the upper pontine region. Correlate with *A*.

CONCLUSIONS AND SUMMARY

The anatomy and angiographic appearance of the pontine arteries are described.

Selective vertebral angiography, with the aid of subtraction, is important for visualization of these small arteries. The incidence of at least some visualization was 87 per cent in the lateral views and 41 per cent in the frontal views of the selective vertebral angiograms in the present material.

The pontine arteries aid in the angiographic localization of the anterior border of the pons but are, in this regard, generally less helpful than the pontomesencephalic veins.

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JUGULAR VENOGRAPHY*

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IN 1968 our colleagues from the Department of Otolaryngology requested jugular venography on several patients. This was a procedure with which we were totally unfamiliar, having seen no description of the technique or results in the radiologic literature. As of this writing several reports on the subject have been published by Swedish authors,[3–7] and the technique has been described by American authors in 2 articles.[2,8] The only report in a radiologic journal is a technical note which describes a catheter approach to the jugular vein from the arm.[1] It is likely that the procedure will be requested more frequently in the future. Although the number of cases we have done is not large, a description of the technique and of our experiences may be of value to other radiologists who are asked to do this procedure.

ANATOMY

The normal appearances are illustrated in Figure 1, *A* and *B*; and 2. From the confluence of sinuses, the transverse sinus passes laterally and anteriorly to the base of the petrous part of the temporal bone. It then becomes the sigmoid sinus which lies in the sigmoid sulcus of the temporal bone, curving downward and medially to the jugular foramen. The superior bulb of the internal jugular vein constitutes its first portion and lies in the posterior compartment of the jugular foramen, separated from the middle ear by a thin plate of bone. The 9th, 10th and 11th cranial nerves pass through the anterior part of the jugular foramen and are therefore in close proximity to the jugular bulb. In the neck the internal jugular vein descends slightly lateral to the internal and common carotid arteries.

Since there are no valves in the upper part of the internal jugular vein or in the dural sinuses, retrograde injection of contrast material will frequently demonstrate the opposite transverse sinus and internal jugular vein as well as the petrosal and cavernous sinuses. Filling of emissary veins at the base of the skull and in the occipital area is a normal occurrence. The right transverse sinus is larger than the left in most individuals and occasionally there may be absence of one transverse sinus and internal jugular vein.

INDICATIONS

Jugular venography is useful in evaluating the presence or extent of tumors in the region of the jugular fossa. The glomera in the region of the temporal bone are rice grain sized structures composed of epithelioid cells in a capillary network surrounded by a thin capsule. They are found in the middle ear and in the adventitia of the jugular bulb. Glomus tumors may therefore arise from the middle ear and produce hearing loss, pulsatile tinnitus and bleeding or from the area of the jugular foramen, in which case there will be interference with the last four cranial nerves. A combination of aural and neurologic signs and symptoms is produced when a tumor has become extensive. It is also possible for these tumors to be multiple and to occur both in the middle ear and adjacent to the jugular bulb. In such a case the treatment might be modified by the findings on the jugular venogram. Over 50 per cent of glomus tumors originate from the jugular bulb. Jugular venography helps to define the extent of the lesion and is especially valuable in the case of a tumor which grows downward in the vein without involving the middle ear or causing bone destruction at the base of the skull. Other tumors which may occur in the region of the jugular foramen include neurofibroma, neurilem-

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moma, chordoma and metastasis. Many otologists believe that this procedure should be routinely performed in all cases suspected of glomus tumor, and all cases of unexplained jugular foramen syndrome.[9]

TECHNIQUE

The sedated patient is placed in the supine position with a pillow under the shoulders and the head tilted back. The skin is marked at the intersection of the common carotid artery and anterior border of the sternocleidomastoid muscle. The vein is distended by occluding its distal part manually or with traction applied to a rubber or plastic sling. Using local anesthesia the skin is punctured at the mark with an 18 gauge thin wall needle. The vein, which is about 1 cm. lateral to the carotid artery, is then punctured and when there is free backflow of blood, a 0.035 inch guide wire is carefully advanced a few centimeters under fluoroscopic control. A polyethylene 240 catheter is then inserted and small injections of contrast material are made manually to check for obstruction and proper catheter position. The catheter may find its way into the common facial vein, in which case it has to be withdrawn and redirected up the jugular vein. If no obstruction is encountered, the catheter tip is placed in the jugular bulb and 40 cc. of meglumine diatrizoate (60 per cent renografin) is injected manually or with a mechanical injector set at a low pressure. The vein must be compressed distally during the injection so that the contrast material will reflux into the dural sinuses. Three roentgenograms are taken in rapid succession. The Towne projection is used for the frontal studies and the head is rotated slightly for the lateral studies to separate the two transverse sinuses. Stenver's views may also be obtained if desired. Following an examination of the roentgenograms, the catheter is removed and the puncture site is compressed for several minutes.

The following brief case reports illustrate some of our experiences with this procedure.

REPORT OF CASES

CASE 1. A 53 year old woman complained of headaches and dizziness. A 2×2 mm. growth, having the appearance of a hemangioma, was present in the external auditory canal next to the tympanic membrane. The normal jugular venogram ruled out hemangioma or glomus tumor of the jugular bulb (Fig. 1, *A* and *B*). The small growth was removed and was indeed

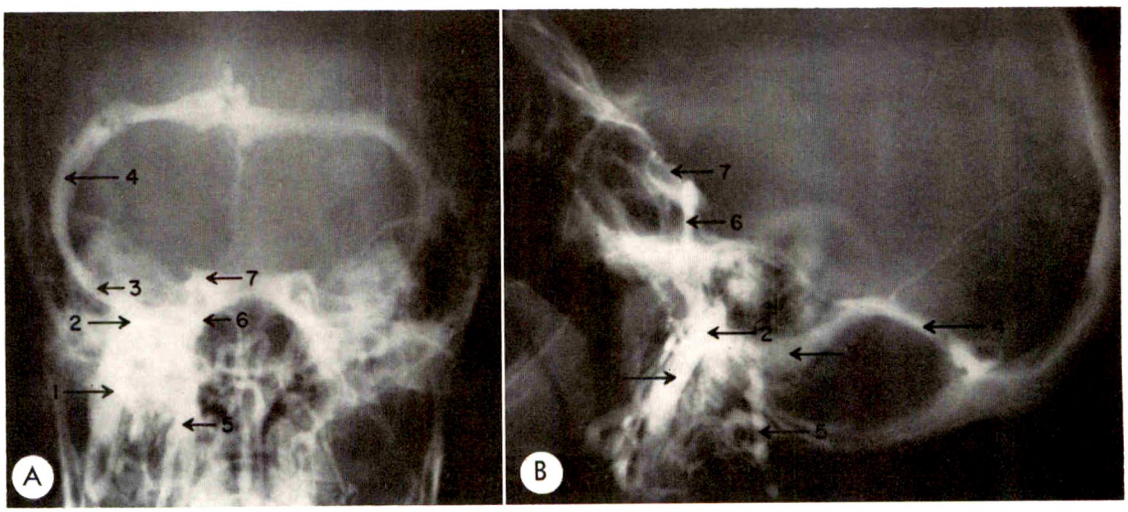


FIG. 1. Case 1. (*A*) Anteroposterior and (*B*) lateral views of normal right internal jugular venogram. There is filling of the opposite transverse sinus by way of the torcular Herophili. 1 = Internal jugular vein; 2 = jugular bulb; 3 = sigmoid sinus; 4 = transverse sinus; 5 = emissary vein; 6 = inferior petrosal sinus; and 7 = cavernous sinus.

a hemangioma. The headaches and dizziness subsided without explanation of their cause.

Case II. This 79 year old woman had gradual hearing loss and pulsations in the right ear for 3 years, with a recent hemorrhage. A 1×1 cm. friable, purplish polyp protruded into the external auditory canal, and there was a loud bruit over the mastoid process. Laminagraphy demonstrated erosion in the area of the jugular foramen. The tumor was partially removed but exploratory tympanotomy was not feasible because of severe bleeding. Histologically the neoplasm proved to be a glomus jugulare tumor. A jugular venogram was then requested with the intention of doing a resection by tympanotomy, in the case of a negative venogram, or radiation therapy if the venogram was positive. On the jugular venogram there was a large filling defect nearly occluding the jugular vein and extending down well below the jugular foramen (Fig. 2). For this reason the patient was referred for radiation therapy, and was given an estimated tumor dose of 6,450 r in 47 days with cobalt 60. The tumor diminished in size and the tympanic membrane healed over it.

Case III. A 29 year old woman complained of hoarseness, difficulty in swallowing, numbness of the right posterior part of the tongue and drooping of the right shoulder. Examination revealed atrophy of the right sternocleidomastoid and trapezius muscles, and right vocal cord paralysis. There was also atrophy of the right side of the tongue with deviation to that side. Laminagraphy disclosed erosion of the right jugular foramen. An exploratory tympanotomy was done with biopsy of a neoplasm in the hypotympanum. In order to better ascertain the extent of the tumor, a jugular venogram was obtained. This demonstrated severe narrowing of the right internal jugular vein down to the level of the atlas (Fig. 3). Because of the extent of the tumor and uncertainty concerning its histology, it was removed by a right cerebellar craniotomy. Histologic examination showed it to be a schwannoma.



Fig. 2. Case II. Glomus jugulare tumor extending down into the internal jugular vein and producing a large filling defect. There is nearly complete occlusion in the area of the jugular bulb.

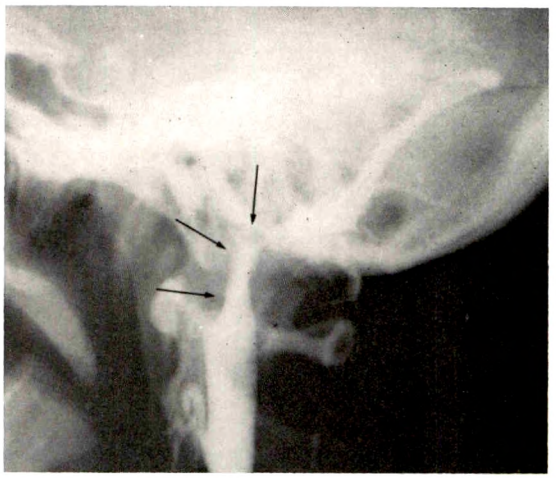


Fig. 3. Case III. Schwannoma of the 11th cranial nerve causing compression of the jugular bulb and proximal internal jugular vein (arrows). Some contrast material gets through into the sigmoid and transverse sinuses.

Case IV. This 39 year old woman had hearing loss on the right with intermittent pain, blockage and drainage of 8 years' duration. Examination revealed bloody discharge and endaural inversion. Laminagraphy suggested enlargement of the jugular foramen. Glomus jugulare tumor was suspected and a jugular venogram was requested to ascertain the extent of the neoplasm. This revealed no filling of the transverse sinus and probable stenosis of the distal sigmoid sinus (Fig. 4). At operation a glomus tumor was found in the middle ear, but it did not extend to the region of the jugular foramen. This was one of our first cases and we believe that the abnormal appearance of the

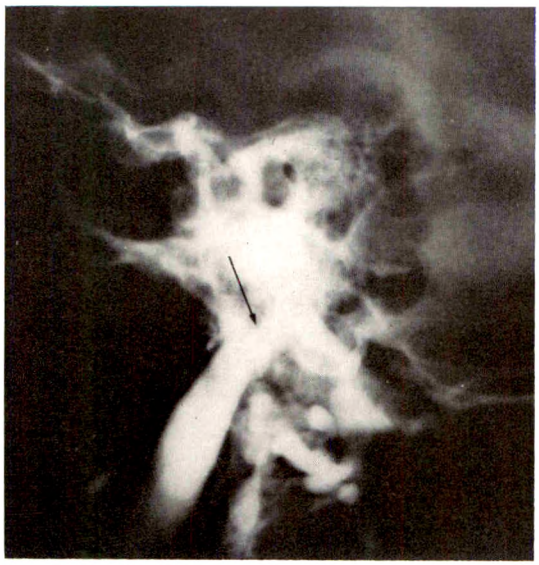


Fig. 4. Case IV. There is no filling of the transverse sinus and poor filling of the sigmoid sinus. Numerous emissary veins are opacified. Immediately above the jugular bulb there is an area of stenosis which was thought to be due to neoplasm (arrow). In actuality, the glomus jugulare tumor was confined to the middle ear. Inadequate compression of the internal jugular vein distally was probably the cause of the misleading appearance.

jugular venogram was probably due to inadequate compression of the distal internal jugular vein as well as injection of an insufficient amount of contrast material.

Case V. A 33 year old woman had a long history of right otitis media with sudden onset of vertigo and right facial paralysis. There was a large central perforation of the tympanic membrane with some white granulation tissue visible. At operation the middle ear was filled with granulomatous material, and a mastoidectomy with facial nerve decompression was done. Postoperatively, healing was not satisfactory and peculiar granulomatous tissue persisted in the area of the operation. The possibility of some type of neoplasm was considered and a jugular venogram was done 4 months postoperatively. This revealed no lesion in the area of the jugular foramen, but because the transverse sinus was not filled, the question of thrombosis was raised (Fig. 5). Four days later extensive aseptic necrosis was found in the region of the middle ear and mastoid, and a radical mastoidectomy was done. The sigmoid and transverse sinuses were not thrombosed.

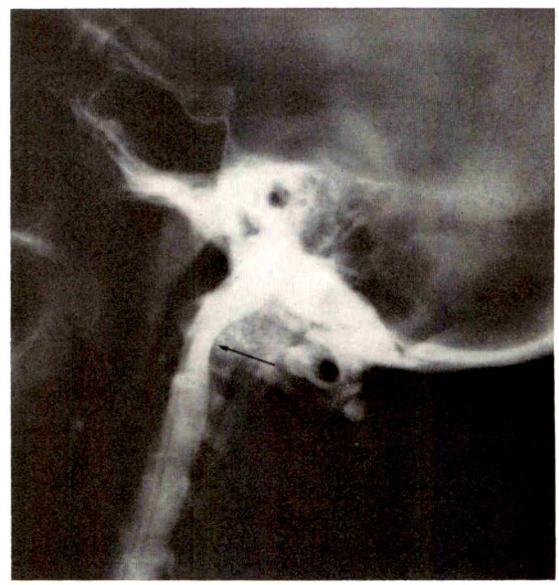


Fig. 5. Case V. Neoplasm in the area of the jugular foramen was ruled out by this study, but the failure of the transverse sinus to fill raised the possibility of thrombosis. At operation no thrombus was found and the lack of filling was probably due to insufficient injection of contrast material. The concavity along the posterior aspect of the proximal internal jugular vein is a normal variant (arrow).

The failure of the transverse sinus to fill was puzzling at the time of the venography. Only 15 cc. of contrast material was injected and we now believe that this is the explanation.

Comment. The last 2 cases are significant because they are examples of partially mistaken diagnosis resulting from improper technique. It is extremely important to compress the distal internal jugular vein so that the contrast material will reflux into the sigmoid and transverse sinuses. In the absence of an obvious obstructive lesion, 30–40 cc. of contrast material must be injected as smaller amounts may be inadequate. Fluoroscopy during insertion of the guide wire and catheter is important in case an obstruction should be encountered and to ensure the proper positioning of the catheter tip.

SUMMARY

Jugular venography is useful in the assessment of the presence or extent of neo-

plasms in the area of the jugular foramen. The indications and technique as well as experiences with 5 cases are described.

The importance of compression of the internal jugular vein distally and injection of a sufficient volume of contrast material is stressed.

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The patients were referred by Brian F. McCabe, M.D., Department of Otolaryngology and Maxillofacial Surgery. Some of the studies were done by Michael D. Sumerling, M.B.

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EXTRA-VENTRICULAR (COMMUNICATING) HYDROCEPHALUS: SOME OBSERVATIONS ON THE MIDLINE VENTRICLES*

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OUR experience with hydrocephalus has indicated the importance of adequate study of the midline ventricles for proper diagnosis and management. The purpose of this communication is to point out and illustrate some of these useful findings.

REVIEW OF THE LITERATURE

A review of the literature concerning hydrocephalus indicates some confusion in terminology and a disagreement concerning etiology.

Dandy and Blackfan[7] introduced the term communicating hydrocephalus to refer to those cases of hydrocephalus where there was free communication between the ventricles and the subarachnoid space. Bucy and Siqueria,[3] and Ransohoff *et al.*[23] criticized the term communicating hydrocephalus because it fails to imply obstruction. Ransohoff and his co-workers[23] suggested the term extra-ventricular hydrocephalus. We prefer this terminology and have prepared Tables I and II to demonstrate the terminology and pathogenesis.

It is believed that most cases of extra-ventricular (communicating) hydrocephalus in infants are due to hemorrhage in the subarachnoid spaces secondary to perinatal trauma and hypoxia.[15,20,26] The roentgenographic aspects of this type of hydrocephalus have been described by Granholm and Radberg.[15] A similar etiology may be detected in adults with subarachnoid bleeding from intracranial aneurysms.[5]

There are two recognized congenital types of extra-ventricular hydrocephalus, the Dandy-Walker malformation[17] and the Arnold Chiari malformation.[3,10,13,19,24,27] The roentgenographic aspects of cerebellar dysplasia (Arnold Chiari) have been well described in recent years.[8,14,22,28]

MATERIAL

The material presented here was investigated at the University of Virginia Hospital during the year 1967, and, except for 3 cases, all were examined during a period of 18 months. Data concerning the size, shape, and position of the 3rd and 4th ventricles and the aqueduct were collected. These findings are discussed in 2 main groups. *Group A* includes 13 cases of cerebellar dysplasia (Arnold Chiari) and 1 case of meningomyelocele, with tentorial block but with no evidence of cerebellar dysplasia. *Group B* comprises 17 cases with obstruction in the subarachnoid spaces of different etiologies.

GROUP A

All patients had meningomyeloceles and were investigated by transcoronal ventriculography. One patient had a myelography as well. Two patients came to autopsy. The roentgen findings and illustrations of the anterior end of the 3rd ventricle in these cases are shown in Figure 1. Lacunar skull was present in 9 cases. In 1 case (G) it was noted that the lacunae, previously seen, had disappeared by the second examination. All cases had variable degrees of aqueduct obstruction, which was complete in 5 cases. One case (G) had partial aqueduct obstruction which became complete following the shunt operation. The pertinent data concerning this group of patients are tabulated in Table III.

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TABLE I

CAUSES OF HYDROCEPHALUS*

Modified from Laurence

I. Overproduction of Cerebrospinal Fluid. Some cases of choroid plexus papilloma
II.† Defective Absorption of Cerebrospinal Fluid? Venous sinus thrombosis. This condition usually produces otitic hydrocephalus with normal or small lateral ventricles but, rarely, this may be associated with dilated lateral ventricles
III. Obstruction of Cerebrospinal Fluid Pathway (most common)
  a. Intra-ventricular
  b. Extra-ventricular
    (i) Tumoral: due to ventricular distortion and displacement
    (ii) Nontumoral (see Table II)

* Not included in this classification is hydrocephalus ex vacuo (simple atrophy). Also excluded is external hydrocephalus which includes otitic hydrocephalus, subdural hygroma and some severe cases of hydrocephalus where the lateral ventricles rupture spontaneously or where cerebrospinal fluid accumulates outside the brain after ventricular tapping.

† Experimental obstruction of the superior sagittal sinus in animals fails to produce any abnormality.[24]

GROUP B

All patients had air studies; 4 of these were pneumoencephalographies and are grouped according to their probable site of obstruction.

Site 1. Obstruction of the exit foramina

TABLE II

CAUSES OF NONTUMORAL EXTRA-VENTRICULAR HYDROCEPHALUS

I. Obstruction of the subarachnoid space and exit foramina
  a. *Aquired*
    1. Hemorrhage
    2. Infection — Bacterial; Tuberculosis; Fungus
    3. Parasite — Toxoplasmosis; Cysticercosis
    4. Abnormal infiltrate — Malignant: Secondary carcinoma; Leukemia; Lymphoma — Nonmalignant: Tuberous sclerosis; Sarcoidosis; Histiocytosis X; Gargoylism
    5.* Excess Proteins in Cerebrospinal Fluid
  b. *Congenital*
    1. Cerebellar dysplasia (Arnold-Chiari malformation)
    2. Dandy-Walker syndrome
    3. ? ? Congenital absence of the subarachnoid space
II. Obstruction outside the cerebrospinal system due to skull abnormalities, *e.g.*, basilar impression and achondroplasia

* This may be associated with choroid plexus papilloma, acoustic neurinoma and, rarely, with some spinal tumors.

of the 4th ventricle (4 cases). The 4th ventricle was markedly dilated.

Site 2. Obstruction mainly in the posterior fossa cisterns (3 cases). The 4th ventricle was slightly dilated and appeared high in position.

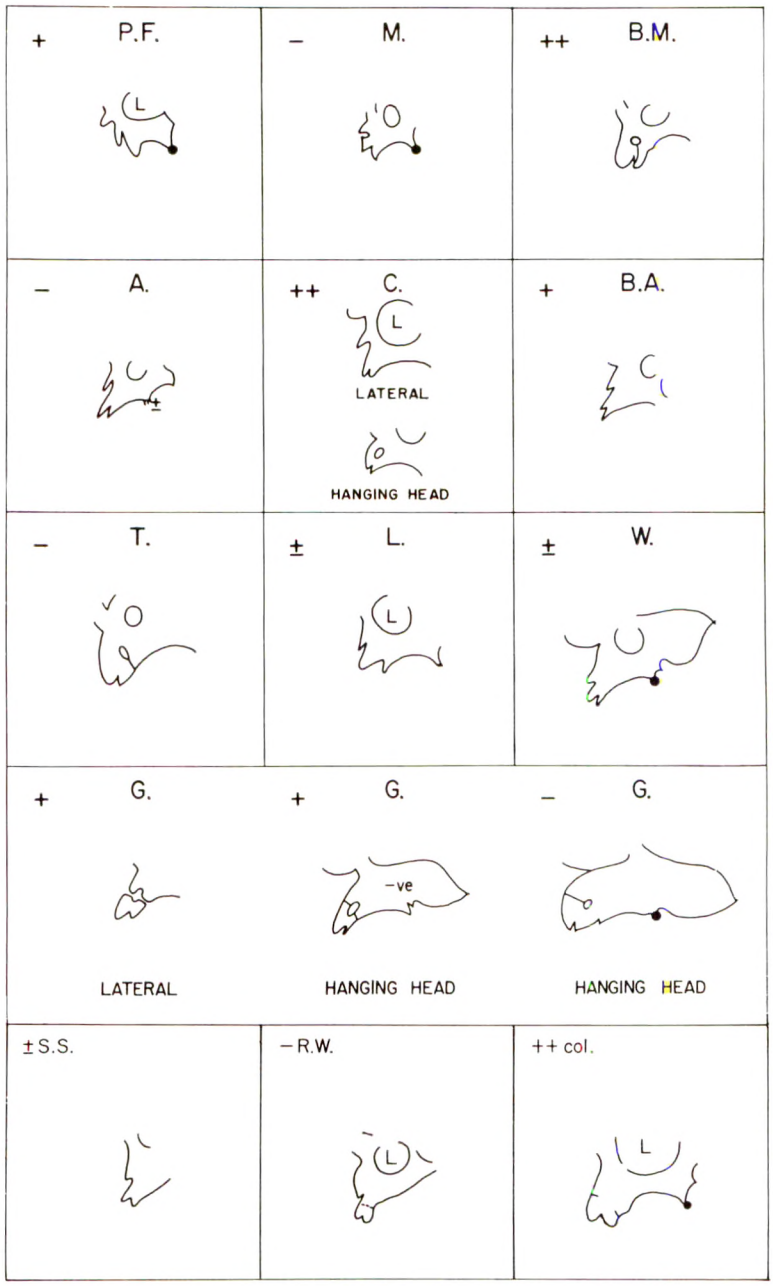


FIG. 1. The appearance of the 3rd ventricle in 13 cases of cerebellar dysplasia (Arnold-Chiari syndrome) is illustrated and some roentgen findings are tabulated.

Lucunar skull represented in the upper corner of every square: –absent; ±mild; +moderate; ++advanced.

Massa intermedia: L=large, more than 10 mm.; –ve=absent.

Aqueduct obstruction: •complete (after repeated attempts); ±apparent complete obstruction (only one attempt).

TABLE III

SUMMARY OF CASES

Group A

Case No.	Age	Sex	Meningomyelocele	Age at Time of Repair of the Meningo-myelocele	Age at Time of Increase of Head Size	Infection of Meninges	Age at First Shunt	Associated Anomalies	Observations
Case 1 (T)	1 da.	F	Thoracolumbar	7 da.	11 da.	—	V.A. 3 wk.	—	4th ventricle adequately shown
Case 2 (G)	6 mo.	M	Lumbar (leaking)	2 da.	1 mo.	+	V.A. 5 wk.	—	4th ventricle well shown; complete aqueduct obstruction following shunt, autopsy done
Case 3 (C)	1 da.	M	Thoracolumbar	1 da.	7 da.	—	V.A. 2 wk.	Bilateral metatarsus varus	4th ventricle shown
Case 4 (L)	3 wk.	F	Lumbar (ruptured)	1 da.	7 da.	—	V.A. 4 wk.	—	4th ventricle adequately shown
Case 5 (B.A.)	5 mo.	F	Lumbar	1 da.	7 da.	—	V.A. 5 mo.	Talipes equinovarus	4th ventricle adequately shown
Case 6 (B.M.)	2 mo.	M	Thoracolumbar	not repaired	3 wk.	—	V.A. 2 mo.	—	Medial part of one lateral ventricle shown herniated in posterior fossa
Case 7 (S.S.)	1 da.	M	Thoracolumbar (leaking)	1 da.	10 da.	—	V.P. 2 wk.	Calcaneal defect of feet; bilateral hydronephrosis	Partial delineation of the 4th ventricle
Case 8 (R.W.)	2 da.	M	Lumbar (leaking)	2 da.	2 wk.	—	V.P. 3 wk.	—	4th ventricle adequately shown
Case 9 (A)	1 wk.	M	Thoracolumbar	2 wk.	1 wk.	—	V.A. 3 wk.	—	Apparent complete aqueduct obstruction (only one attempt); possible cerebellar dysplasia
Case 10 (P.F.)	1 wk.	M	Thoracolumbar (leaking)	1 da.	1 da.	+	V.P. 2 wk.	Urinary tract infection	Complete aqueduct obstruction; probable cerebellar dysplasia
Case 11 (M)	1 da.	F	Lumbar	1 da.	1 wk.	—	V.A. 2 wk.	—	Complete aqueduct obstruction; possible cerebellar dysplasia
Case 12 (W)	2 da.	F	Lumbosacral	2 da.	1 da.	—	V.P. 1 wk.	Bilateral hip dislocation	Complete aqueduct obstruction; probable cerebellar dysplasia
Case 13 (Col)	3 wk.	M	High dorsal	8 mo.	1 da	—	V.A. 7 wk.	Bilateral hip dislocation and talipes equinovarus	Complete aqueduct obstruction; autopsy done; cerebellar dysplasia
Case 14 (S.C.)	2 mo.	F	Low lumbar	1 da.	7 da.	—	Not done	—	Pseudodiverticulum 3rd ventricle and no evidence of cerebellar dysplasia

V.A. = ventriculoatrial; V.P. = ventriculoperitoneal.

Site 3. Tentorial obstruction (7 cases).

Site 4. Obstruction at the tentorium and sylvian fissures (3 cases). The pertinent data concerning this group of patients are summarized in Table IV.

RESULTS AND DISCUSSION

GROUP A: CEREBELLAR DYSPLASIA

1. *Plain skull* roentgenograms revealed lacunar skull in some cases but none had abnormality at the craniocervical junction. This was also the experience of Kruyff and Jeffs[18] in infants and children. In the adult type, however, anomalies at the craniocervical junction are fairly common.[8]

2. *Third ventricle*: 12 cases had a deformity of the anterior end of the 3rd ventricle. This was first described by Gooding *et al.*[14] as a transventricular connexus inferior to the anterior commissure which may present as a pseudodiverticulum of the lamina terminalis. They found the same deformity in 1 of 19 cases of congenital aqueduct

TABLE IV

SUMMARY OF CASES

Group B

Case No.	Age	Sex	Clinical Picture	Roentgen Findings	Surgical Procedures and Pathologic Findings	Diagnosis
Site 1 Case 15 (G.J.)	8 mo.	M	Large head at birth; born by uncomplicated cesarean section	*Transcoronal ventriculogram:* (Fig. 8, *A–D*)	Posterior fossa exploration; partial removal of cystic 4th ventricle followed by atrioventricular shunt	Dandy-Walker malformation
Case 16 (S.P.)	6 wk.	F	Fever at age of 11 days with stiff neck	*Transcoronal ventriculogram:* cloudy cerebrospinal fluid, no air could be passed outside 4th ventricle (Fig. 9, *A* and *B*)	V.A. shunt when cerebrospinal fluid was clear	Post infection obstruction of the 4th ventricle exit foramina
Case 17 (Y.T.)	37 yr.	M	1 month history of headache and vomiting; stuporous on admission	*Ventriculogram:* dilated anterior 3rd ventricle, marked dilatation of 4th ventricle which lay well above the foramen magnum; aqueduct was dilated and slightly kinked forward	Posterior fossa exploration: no tumor was found; adhesions and loculated fluid below the 4th ventricle; histologic examination of a biopsy from the meninges showed evidence of inflammation	Meningitis obliterating the 4th ventricle exit foramina
Case 18 (L.J.)	14 yr.	M	4 week history of fever, headache, vomiting and neck stiffness; lumbar puncture showed cloudy cerebrospinal fluid	*Ventriculogram:* anterior end of the 3rd ventricle was markedly dilated (Fig. 10, *A* and *B*)	V.A. shunt	Meningitis with obstruction of the 4th ventricle exit foramina and cyst formation
Site 2 Case 19 (D.D.)	3 yr.	F	Fever and splenomegaly 3 months before admission; had negative tuberculin test; cerebrospinal fluid proteins were 288 mg. per cent, and 330 cells 75 per cent of which were polymorphonuclear cells	*Ventriculogram:* dilatation of the optic recess of the 3rd ventricle, aqueduct was dilated, 4th ventricle moderately dilated (Fig. 11, *A* and *B*)	*Autopsy:* ventriculitis with adhesions along the inferior surface of cerebellum, cerebral peduncles and front of pons	Tuberculous meningitis with disseminated tuberculosis involving lungs, liver, and kidney; diagnosis made by culture and histology
Case 20 (H.M.)	17 mo.	M	Increasing head size, fever and stiff neck; the patient was incubated for few days after birth for respiratory difficulty; lumbar puncture showed cloudy cerebrospinal fluid; fever rose following the ventriculography	*Ventriculogram:* (Fig. 12)		Probable cystic meningitis in the posterior fossa
Case 21 (K.M.)	1 da.	F	Mother had ante and postpartum hemorrhage with difficult labor and blood transfusion was given to infant (hematocrit 30 per cent); 10 days after delivery head started to increase in size	*Transcoronal ventriculogram:* high 4th ventricle with dilated posterior fossa cisterns producing reversed tentorial herniation (Fig. 13, *A* and *B*)	V.P. shunt	Posterior fossa adhesions with high 4th ventricle
Site 3 Case 22 (V.N.)	3 wk.	F	Large head and tense fontanelles	*Transcoronal ventriculogram:* (Fig. 14, *A* and *B*)	V.A. shunt complicated by bilateral subdural hematoma; patient died but no autopsy done	Tentorial block of questionable etiology
Case 23 (O)	5 mo.	M	Progressive head enlargement	*Transcoronal ventriculogram:* agenesis of the corpus callosum; 3rd ventricle had a large diverticulum arising from its superior surface lying between the cerebral hemispheres. A repeat transcoronal ventriculogram 5 months later (Fig. 15*B*) showed evidence of tentorial block with increased dilatation of the lateral ventricle, also of the 3rd ventricular diverticulum	V.A. shunt	Agenesis of the corpus callosum with tentorial block of questionable etiology
Case 24 (C.T.)	4 wk.	M	Increasing head size; patient was delivered by high forceps after artificial rupture of the membranes; mother had fever and vomiting on 39th week of pregnancy	*Transcoronal ventriculogram:* there was agenesis of the corpus callosum; the anterior 3rd ventricle was normal (Fig. 15*A*)	V.P. shunt	Agenesis of the corpus callosum with tentorial block of questionable etiology

V.A. = ventriculoatrial; V.P. = ventriculoperitoneal.

TABLE IV (*Continued*)

Case No.	Age	Sex	Clinical Picture	Roentgen Findings	Surgical Procedures and Pathologic Findings	Diagnosis
Case 25 (F.R.)	3 mo.	M	Premature baby who had increasing head size and projectile vomiting; his mother had vaginal bleeding at 1 and 7½ months of pregnancy; the baby required hospitalization for 5½ weeks after delivery	*Transcoronal ventriculogram:* marked dilatation of the anterior 3rd ventricle; normal 4th ventricle. There was evidence of tentorial block with large cisterna velum interpositum. Repeat *Transcoronal ventriculogram* 7½ months later showed increase in dilatation of both lateral and 3rd ventricles and there was complete aqueduct obstruction	V.P. shunt	Tentorial block of questionable etiology; aqueduct obstruction following shunt procedure
Case 26 (St.C.)	35 yr.	M	3 month history of compound fracture of left frontal bone; 2 month history of headache, vomiting and obtundation; culture of cerebrospinal fluid grew *Nocardia asteroides*	*Carotid arteriograms:* narrowing of the subarachnoid portions of the carotids as in cases of tuberculous meningitis (Greitz[16]). *Ventriculogram:* the 4th ventricle was normal (Fig. 16, *A-D*)	Posterior fossa exploration showed some arachnoid adhesions; biopsy and culture were done; autopsy showed gray plastic exudate 2 cm. thick mainly in the interpeduncular region; there was a small abscess in the hypothalamus	Post-traumatic *Nocardia* (fungus) meningitis
Case 27 (F.V.)	54 yr.	F	Long history of headache and vomiting and neck pain	*Vertebral angiograms:* backward displacement of the upper part of the basilar artery; the right posterior cerebral artery did not fill (Fig. 17, *A-D*)	Posterior fossa exploration showed some arachnoid adhesions; right postcommunicating artery was clipped with no complication	Tentorial block associated with an aneurysm arising from the right posterior cerebral artery with a clot producing an unusual hourglass sella
Case 28 (R.R.)	24 yr.	M	At the age of 2½ months had progressive head enlargement, proceeded to grow fairly normally and attended school through the 3rd grade; 3–4 weeks before admission he had leg weakness with nausea and vomiting; the optic disks were flat and pale	*Plain skull roentgenograms:* large head with fusion of the sutures; the sella was oblong in shape with thick lamina dura; the appearance was consistent with longstanding, intermittent hydrocephalus. *Pneumoencephalogram:* (Fig. 18, *A-C*)	No shunt was done	Tentorial block of questionable etiology; arrested hydrocephalus
Site 4 Case 29 (W.W.)	19 yr.	M	3 year history of headache with nausea and vomiting; mumps encephalitis at age 3½ years	*Pneumoencephalogram:* anterior 3rd ventricle was markedly dilated resting on the dorsum sellae; there was evidence of tentorial block; 4th ventricle was normal		Occult hydrocephalus; mumps encephalitis at age of 3½ years
Case 30 (H.M.)	50 yr.	M	Depressed, patient was also disoriented and ataxic; there was positive Romberg's sign; cerebrospinal fluid pressure was normal	*Pneumoencephalogram:* only small amount of air noted in the sylvian fissures but no air seen over the cerebral hemispheres (Fig. 19, *A* and *B*)	V.A. shunt followed by considerable improvement mentally	Occult hydrocephalus; tentorial block of questionable etiology
Case 31 (T.H.)	63 yr.	M	Dementia, disorientation; cerebrospinal fluid proteins 75 mg. per cent, cerebrospinal fluid pressure =200 mm. cerebrospinal fluid	*Pneumoencephalogram:* the lateral ventricles were dilated; the anterior 3rd ventricle was normal; there was a high basilar artery indenting the 3rd ventricle floor; air accumulated in large pontine and suprasellar cisterns, also in sylvian fissures and callosal cisterns delineating the anterior and middle cerebral artery branches; no air was seen over the cerebral hemispheres	V.A. shunt with obvious improvement 2 months later; intrathecal scan showed marked delay in the uptake in the posterior fossa and in the sylvian fissures	Occult hydrocephalus

stenosis. Case 14 had the same deformity with no evidence of cerebellar dysplasia.

In the present study 4 patients showed a filling defect within the anterior 3rd ventricle above the chiasm. In 1 patient, Case 3 (C), what appeared to be a diverticulum of the lamina terminalis, in another view with more air in the 3rd ventricle, was shown to be a filling defect behind the lamina terminalis (Fig. 1; and 5, *A* and *B*). It appears that the pseudodiverticulum and the anterior filling defect seen in air studies represent one anatomic lesion—an accessory transventricular coronal connexus.

If it lies close to the lamina terminalis it may only be partly outlined with air, producing an apparent diverticulum of the lamina terminalis.

The massa intermedia was large (over 1 cm.) in 5 cases. Gooding *et al.*[14] and McCoy *et al.*[22] also found large massa intermedia in a fair number of patients with cerebellar dysplasia. This finding, however, is not as specific for cerebellar dysplasia as the deformity of the anterior 3rd ventricle.[14]

3. *Aqueduct obstruction*: All 13 cases of cerebellar dysplasia had variable degrees of aqueduct obstruction. This was best shown in the hanging head position with the infant held by his feet upside down for a few minutes. Eight patients had partial aq-

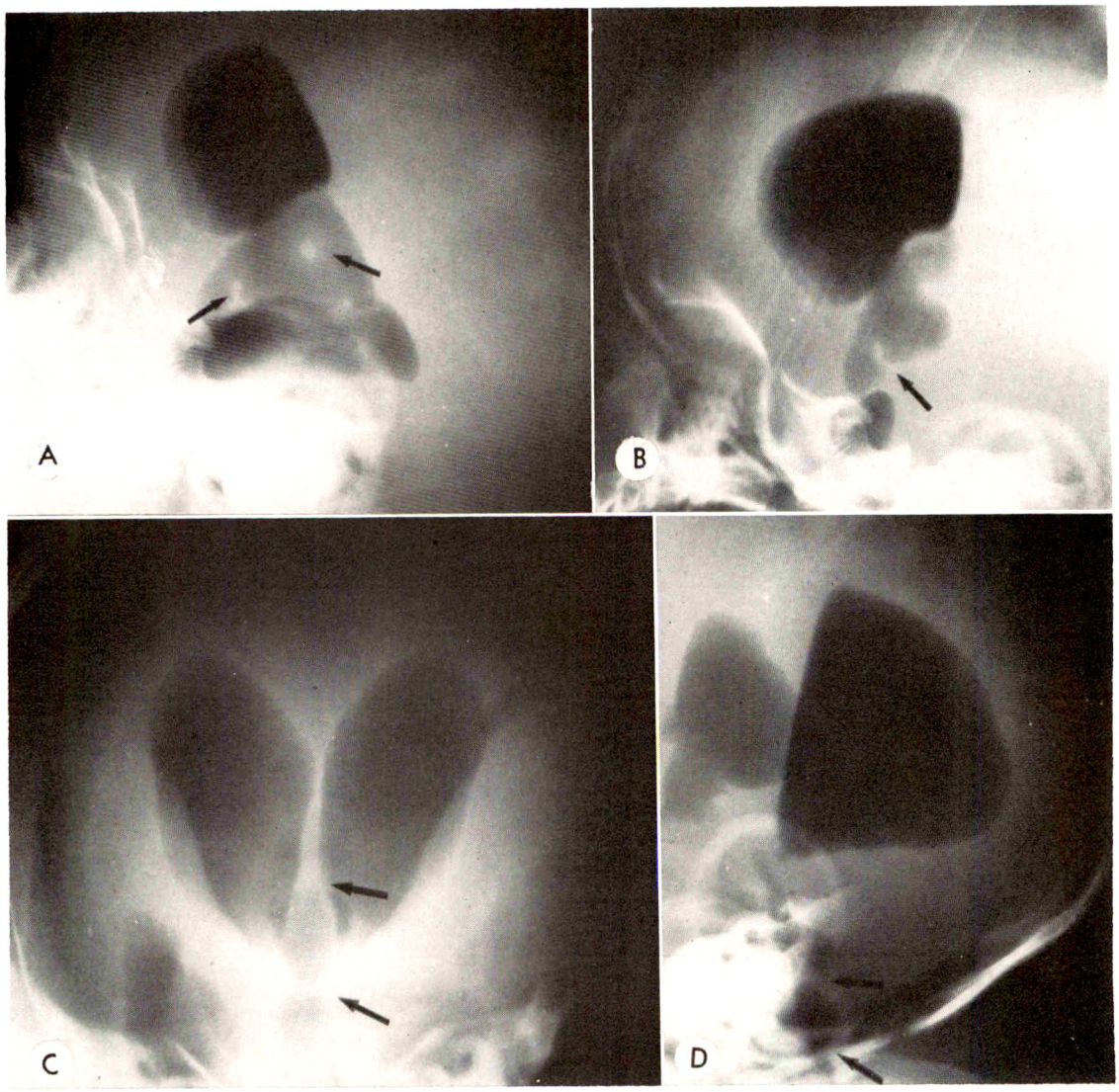


FIG. 2. Case 1. (*A*) Note 2 defects in the 3rd ventricle, the massa intermedia and an accessory transventricular connexus (arrows). (*B*) The accessory connexus appears to have an attachment to the floor of the 3rd ventricle behind the infundibular recess (arrow). (*C*) Towne's view showing the massa intermedia and the accessory connexus (arrows). (*D*) Brow-down position showing the dilated posterior 3rd ventricle, flattened cisterna magna, and the elongated 4th ventricle with its lower part below the foramen magnum. Note the double hump appearance of its posterior border (arrows).

ueduct obstruction. Some had apparent complete obstruction which on repeated attempts showed the air to pass, delineating the 4th ventricle. One case had equivocal complete aqueduct obstruction. Five cases had complete aqueduct obstruction; one of these developed complete obstruction following shunt operation (Case 2; Fig. 3, *A–E*). This secondary type of aqueduct obstruction was first reported by Foltz and Shurtleff.[12]

The etiology of aqueduct obstruction in cases of cerebellar dysplasia is still controversial, but there appears to be more than one etiology. Doran and Guthkelch[10] and McCoy *et al.*[22] believe that it is due to squeezing of the mid and hind brain in a small posterior fossa (encephalocranial disproportion).

McCoy and co-workers[22] showed in postmortem contrast studies that apparent complete aqueduct obstruction, *in situ*, was relieved when the brain was removed from the skull.

4. *Fourth ventricle*: This was well outlined in 5 cases, showing a double hump appearance of its posterior border (Fig. 2*D*); this appearance was first described by McCoy *et al.*[22] They attributed it to bulging of the vermis into the elongated 4th ventricle. In 2 cases the lower end of the 4th ventricle appeared to represent an extension into a wide central canal of the spinal cord (Fig. 6*A*).

GROUP B

Laurence[19] showed, by special postmortem examination, considerable dilatation of the subarachnoid spaces in the cranial cavity below the site of the subarachnoid obstruction. Craig[6] and Russell[24] described the pathologic appearance of cystic arachnoiditis. Granholm and Radberg[15] showed, in air studies, the dilatation of the subarachnoid cisterns in some cases of extra-ventricular hydrocephalus. Our studies in this group confirm and amplify these findings.

1. *The 4th ventricle* was markedly dilated, in this group, when the obstruction was at or near the exit foramina. Only in the case of Dandy-Walker syndrome (Fig. 8, *A–D*) did the 4th ventricle reach the foramen magnum. Also in this case the 4th ventricle was shown to be patent in the first examination, but following the posterior fossa exploration and the shunt procedure, the second ventriculography showed complete obstruction of the 4th ventricle. Gardner[13] has pointed out that the membranes over the exit foramina in some of these cases may be semipermeable, and their function may only be upset later in life.

Because acquired inflammation near the exit foramina may be more diffuse, associated dilatation of the lower posterior fossa cisterns would prevent the dilated 4th ventricle from reaching the foramen magnum. Therefore, it can be stated that if a dilated 4th ventricle is seen at or below the foramen magnum, the possibility of Dandy-Walker syndrome should be considered.

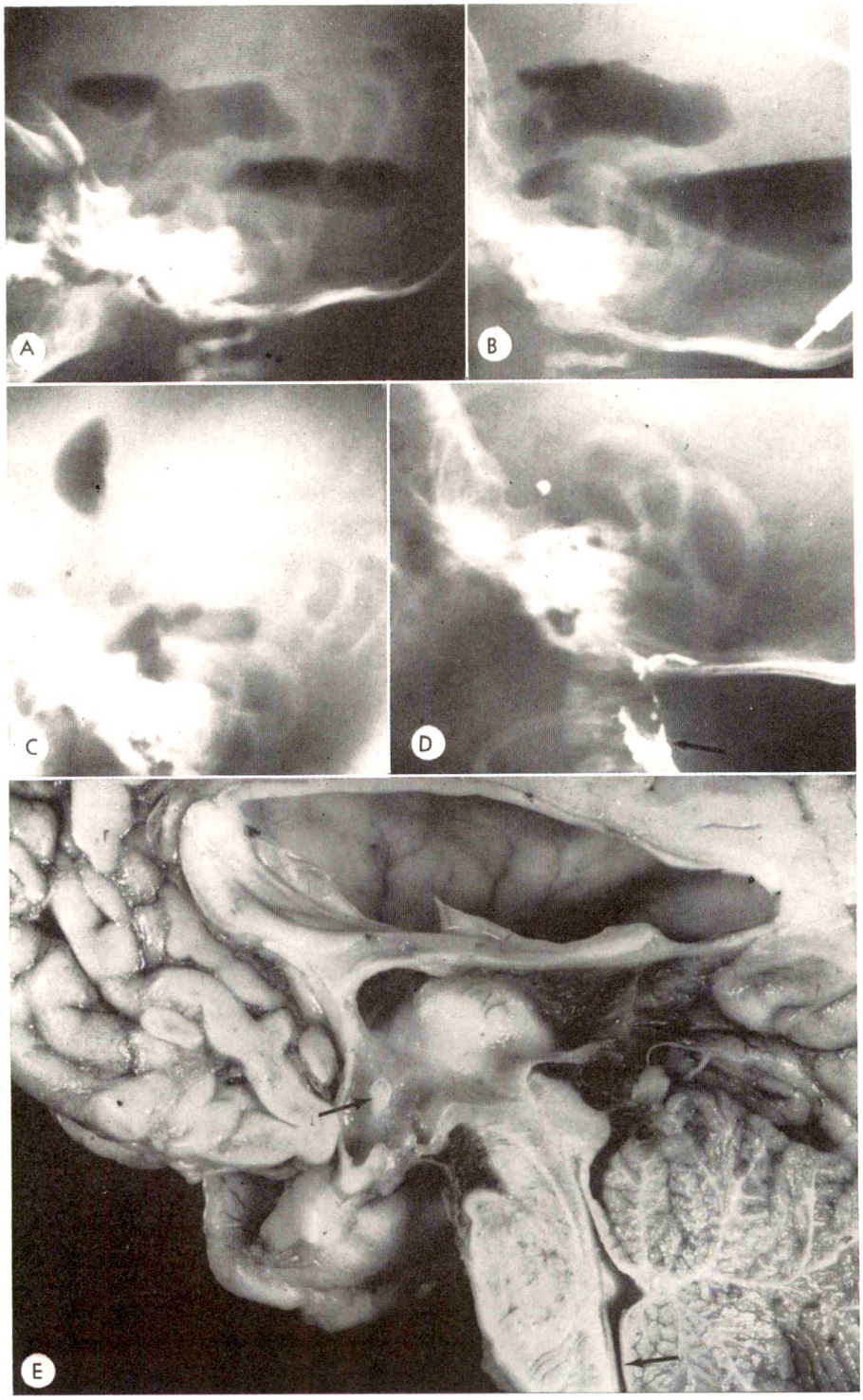
In cases of cystic arachnoiditis of the posterior fossa (Cases 19, 20 and 21), the 4th ventricle was slightly dilated and appeared high in position.

When the subarachnoid obstruction was mainly at or above the tentorium, the 4th ventricle appeared normal or was only slightly dilated.

2. *The aqueduct* was shown to be dilated in 7 cases; its lower part was assimilated in the cavity of markedly dilated 4th ventricle in 4 cases and was slightly kinked in 2 of these cases.

3. *Third ventricle*: (a) The anterior end of the 3rd ventricle was dilated in almost all cases in Group B. A dilated anterior 3rd ventricle usually indicates obstruction to the flow of the cerebrospinal fluid. In contrast, simple atrophy may cause dilatation of the body of the 3rd ventricle in its transverse diameter, but the anterior in-

ferior part remains small and collapsed. This is due to the fact that atrophy produces passive dilatation due to brain tissue loss. The brain tissue in relation to the anterior 3rd ventricle is quite thin (Fig. 4) and, if it degenerates, will not produce



appreciable secondary dilatation. It is very rare for simple atrophy to produce dilatation of the anterior 3rd ventricle.[21] We believe that dilatation of the anterior end of the 3rd ventricle, when present, is a useful differential point, particularly in cases of occult hydrocephalus where shunt operation is very useful.[1] The use of intrathecal scanning[2,9] provides further differential information.

In cases of hydrocephalus, the optic recess usually dilates first; later there is enlargement of both recesses with forward bowing of the lamina terminalis. In advanced long-standing cases the anterior end appears balloon-like (Fig. 9, *A* and *B*; and 18, *A B*, and *C*).



Fig. 4. Sagittal section of a normal 3rd ventricle showing the massa intermedia and the anterior commissure (arrows).

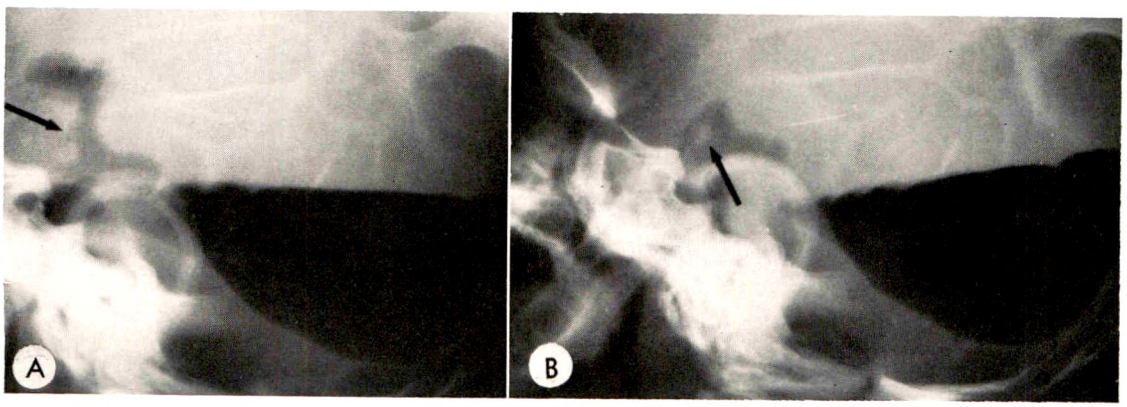


Fig. 5. Case 3. (*A*) Pseudodiverticulum is noted in the lamina terminalis (arrow). (*B*) More air in the 3rd ventricle demonstrates an intraventricular defect. This case shows that when the accessory connexus is close to the lamina terminalis, it may only be partly delineated with air, giving a pseudodiverticulum appearance.

Fig. 3. Case 2. (*A*) Preoperative ventriculogram shows lacunar skull, no massa intermedia. The accessory connexus is seen. (*B*) Post-shunt ventriculogram. The lacunar skull is no longer present. There is more dilatation of the anterior part of the 3rd ventricle, and forward bowing of the lamina terminalis can be seen. Also, there is atrophy of the accessory connexus, the pineal recess having been assimilated in the suprapineal recess. There is complete aqueduct obstruction. (*C*) Preoperative ventriculogram. The air coaxed into the subarachnoid space, on turning the patient on his back, accumulated in front of the pons with evidence of tentorial block. (*D*) Post-shunt myelogram shows marked obstruction in the upper cervical region with a well defined elongated filling defect produced by the herniated vermis and by the kinked medulla. Note the reversed curve of the occipital bone and the disappearance of the lacunar skull. (*E*) Sagittal section through the midline ventricles showing the accessory connexus in the anterior part of the 3rd ventricle (arrow). The 4th ventricle was elongated with cerebellum bulging in its posterior part giving the double hump appearance noted on the air studies (arrow). There was no massa intermedia and the aqueduct was obstructed. Note the beaking of the quadrigeminal plate.

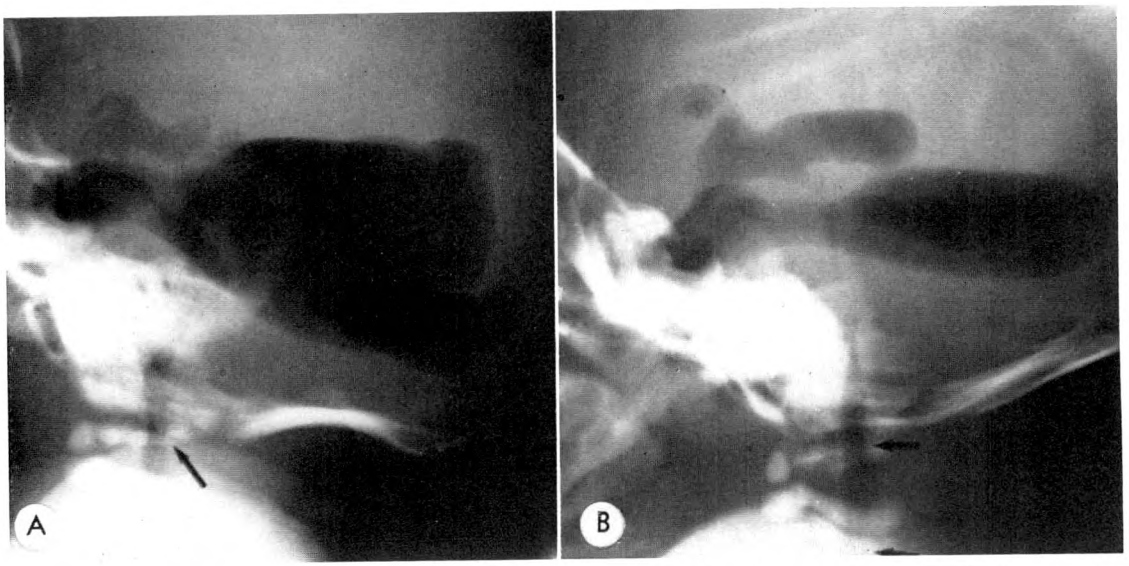


FIG. 6. Case 4. (*A*) The 4th ventricle is elongated and extends to the upper cervical canal. Its lower end is most probably represented by a dilated central canal of the upper cervical cord (arrow). Case 5. (*B*) Another example of an elongated low 4th ventricle with a double hump appearance in its posterior border (arrows).

(b) A dilated anterior 3rd ventricle lying far away from the sella in children of this group was shown to be associated with dilatation of the suprasellar cistern (Fig. 14, *A* and *B*). This may suggest that the obstruction in the subarachnoid space has extended beyond the posterior fossa. This is in contrast to the close application of the dilated 3rd ventricle usually seen in other types of cerebrospinal fluid obstruction. The distance from the tuberculum sellae and the optic chiasm varies from 10–23 mm. normally.[4] Displacement of the 3rd ventricle was shown to be due to

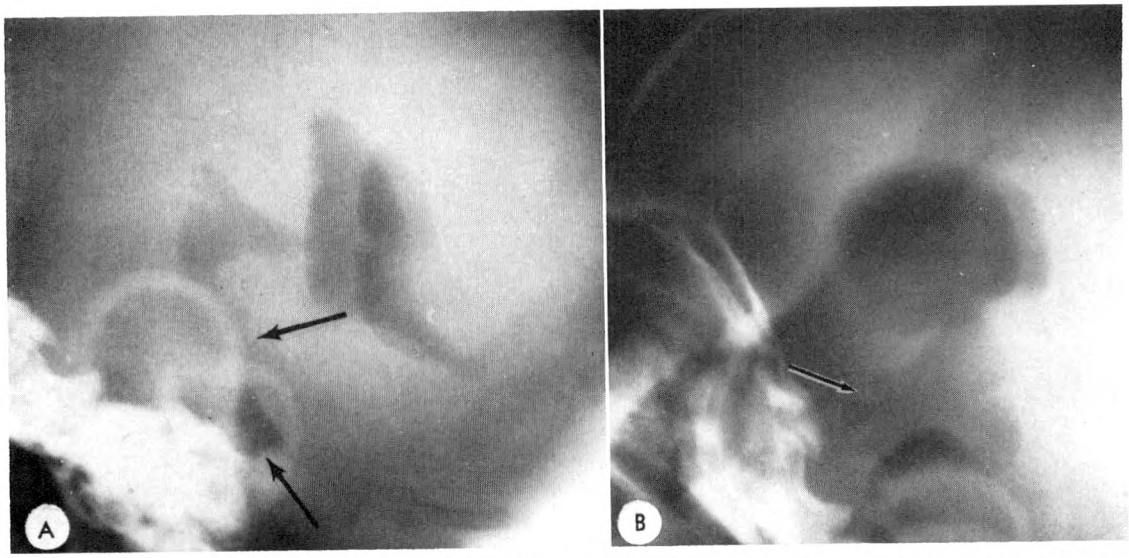


FIG. 7. Case 14. Meningomyelocele with tentorial block. (*A*) Normal appearance of the aqueduct, 4th ventricle and cisterna magna (arrows). (*B*) Pseudodiverticulum in the lower part of the lamina terminalis (arrow).

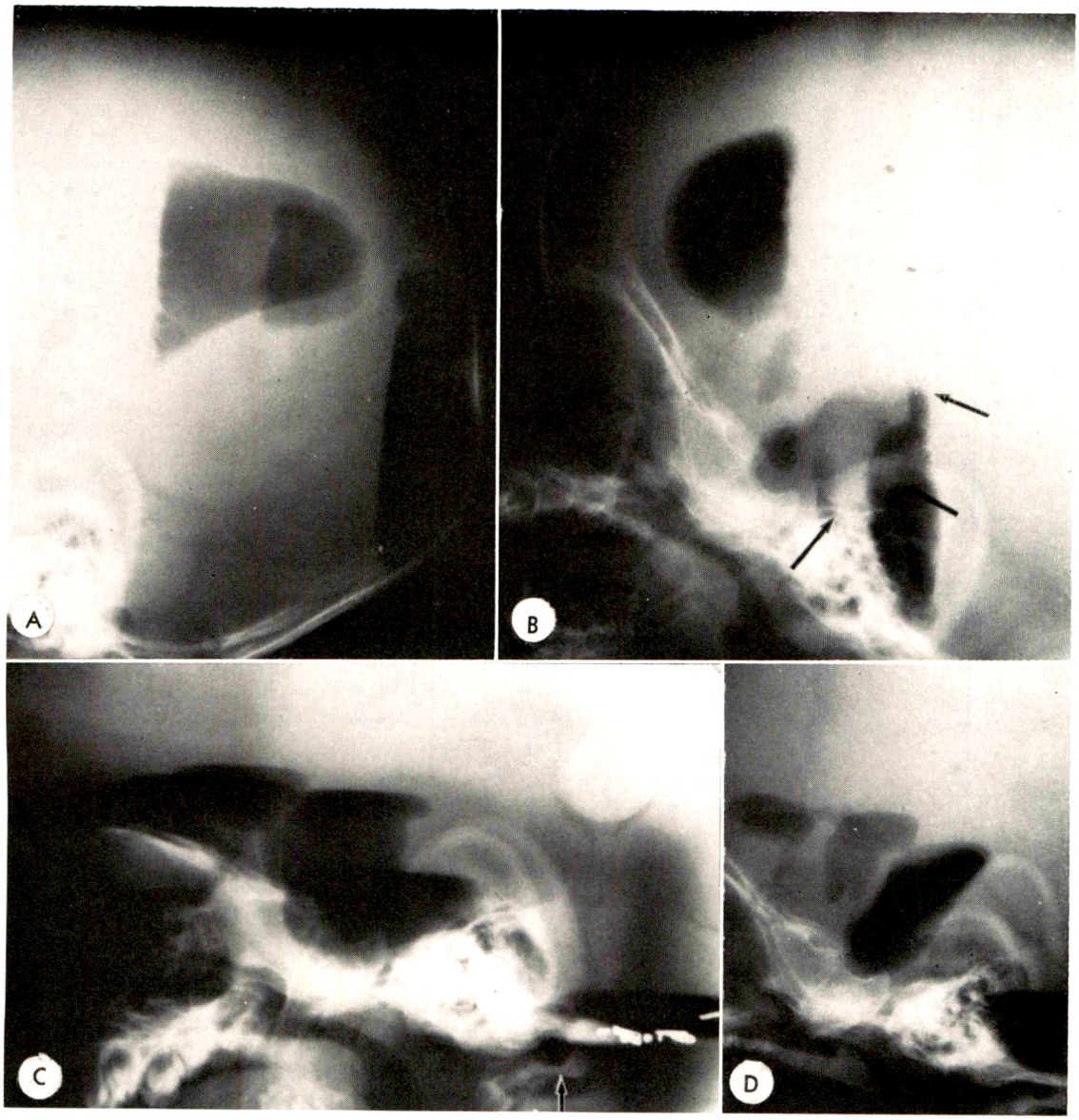


Fig. 8. Case 15. Dandy-Walker syndrome. (*A*) Note the elevation of the posterior parts of the lateral ventricles, also note air in a huge 4th ventricle. (*B*) Brow-up view following the hanging-head position. Note air in the dilated aqueduct (upper arrow). The brain stem is well outlined by air in the pontine cistern and in the anterior part of the large 4th ventricle, which was partially patent (arrows). (*C*) Postoperative ventriculogram. The 4th ventricle is completely obstructed at this time, its lower part is herniated in the upper cervical region (arrow). There is also marked ballooning of the anterior end of the 3rd ventricle. (*D*) Preoperative ventriculogram. The anterior end of the 3rd ventricle appears normal in position. There is only mild dilatation of its optic recess. Note air in the huge 4th ventricle reaching the foramen magnum.

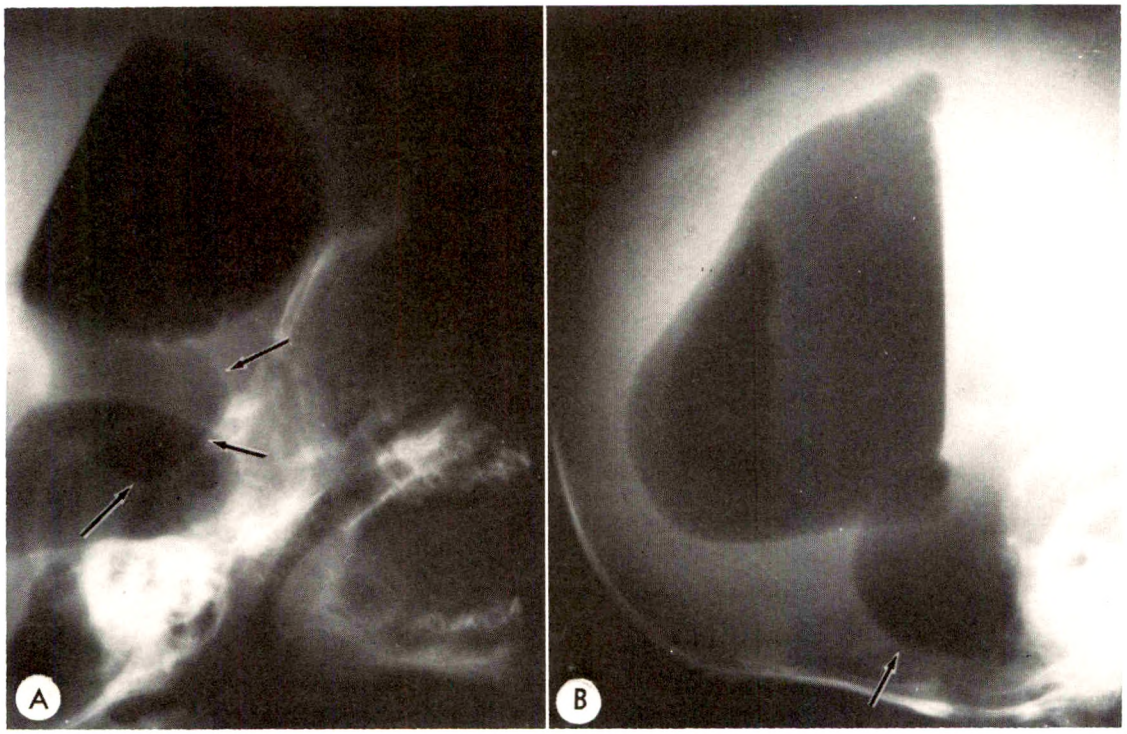


FIG. 9. Case 16. (*A*) Note the ballooning of the anterior end of the 3rd ventricle lying on the sella (arrows). (*B*) Huge 4th ventricle, note that it does not reach the foramen magnum (arrow).

an aneurysm in one of our adult patients (Fig. 17, *A–D*).

(c) A defect in a dilated 3rd ventricle was shown in a case of nocardia meningitis with an inflammatory mass in the floor of the 3rd ventricle (Fig. 16, *A–D*). The same defect can be produced by basilar artery aneurysm with extra-ventricular

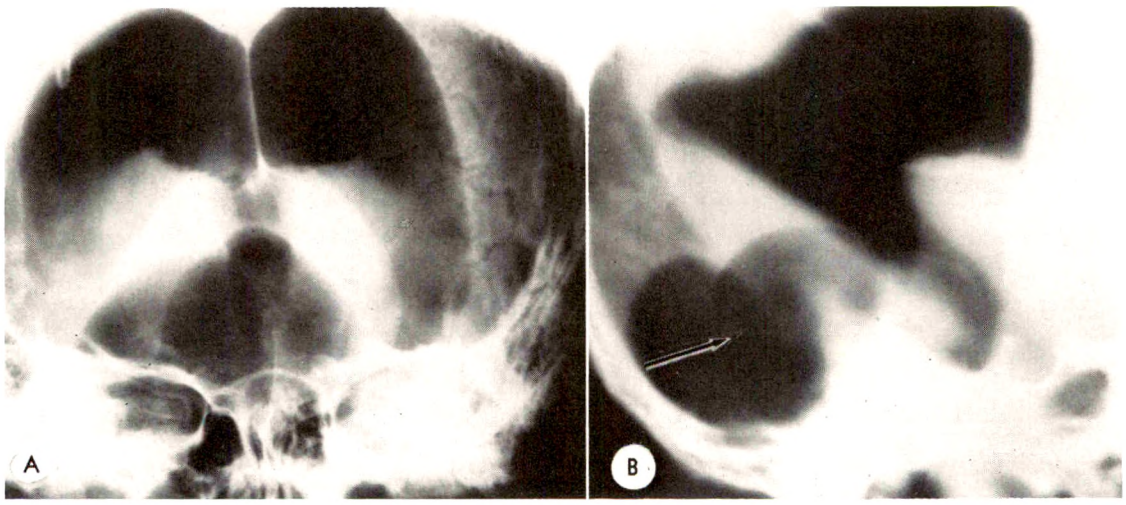


FIG. 10. Case 18. (*A*) Advanced dilatation of the 4th ventricle lying in the midline. Note the large air-filled space on its right side. (*B*) The posterior inferior surface of the 4th ventricle can be seen lying well above the foramen magnum (arrow). The aqueduct is assimilated in the dilated 4th ventricle. The loculated cystic space is noted to lie behind the 4th ventricle.

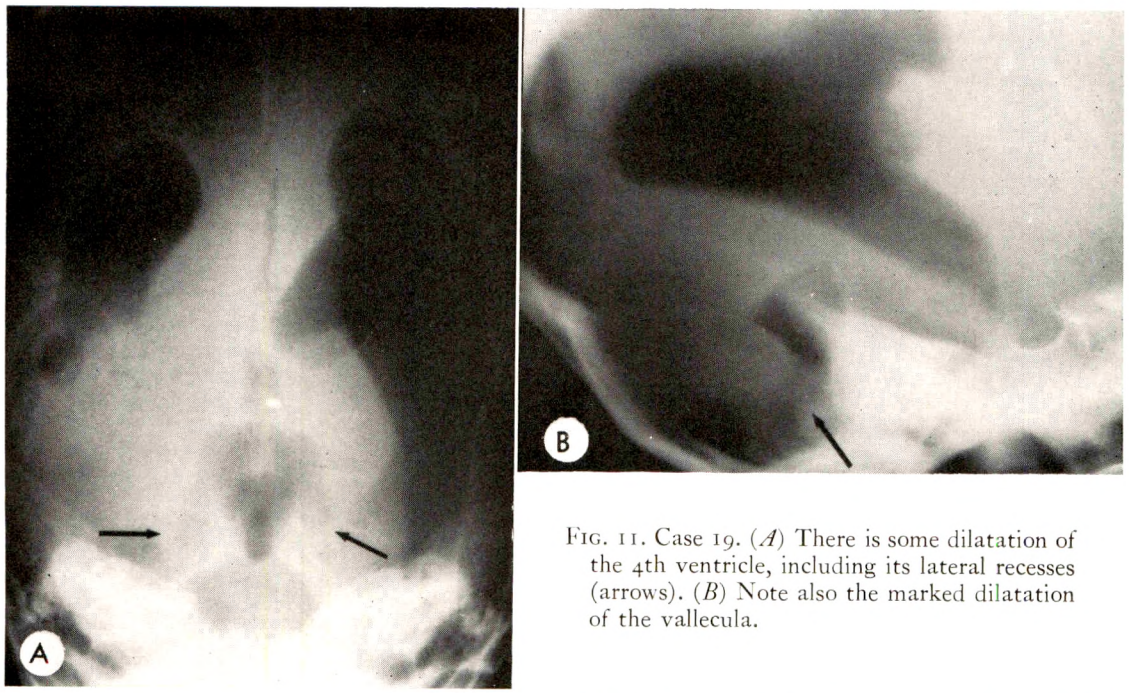


FIG. 11. Case 19. (*A*) There is some dilatation of the 4th ventricle, including its lateral recesses (arrows). (*B*) Note also the marked dilatation of the vallecula.



FIG. 12. Case 20. There is some elevation of the 4th ventricle. This is shown in the hanging-head position (arrow). Note also the dilated posterior fossa subarachnoid spaces (arrow).

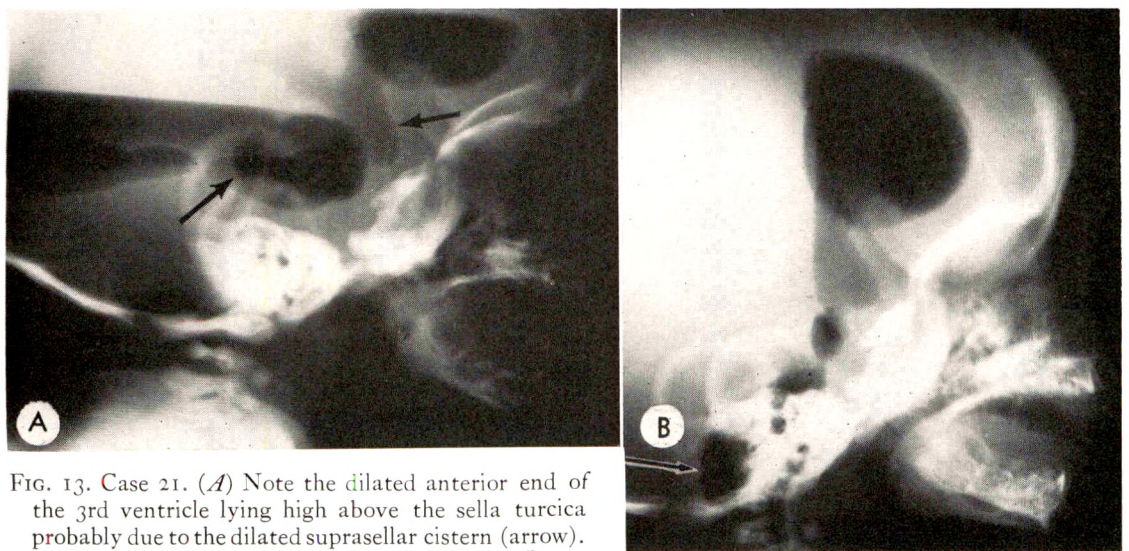


FIG. 13. Case 21. (*A*) Note the dilated anterior end of the 3rd ventricle lying high above the sella turcica probably due to the dilated suprasellar cistern (arrow). Also note the high position of the 4th ventricle, probably displaced by the dilated posterior fossa cisterns (arrow). (*B*) Brow-up view after the hanging-head position showing the dilated posterior fossa cistern (arrow); also, the suprasellar cistern shows some dilatation.

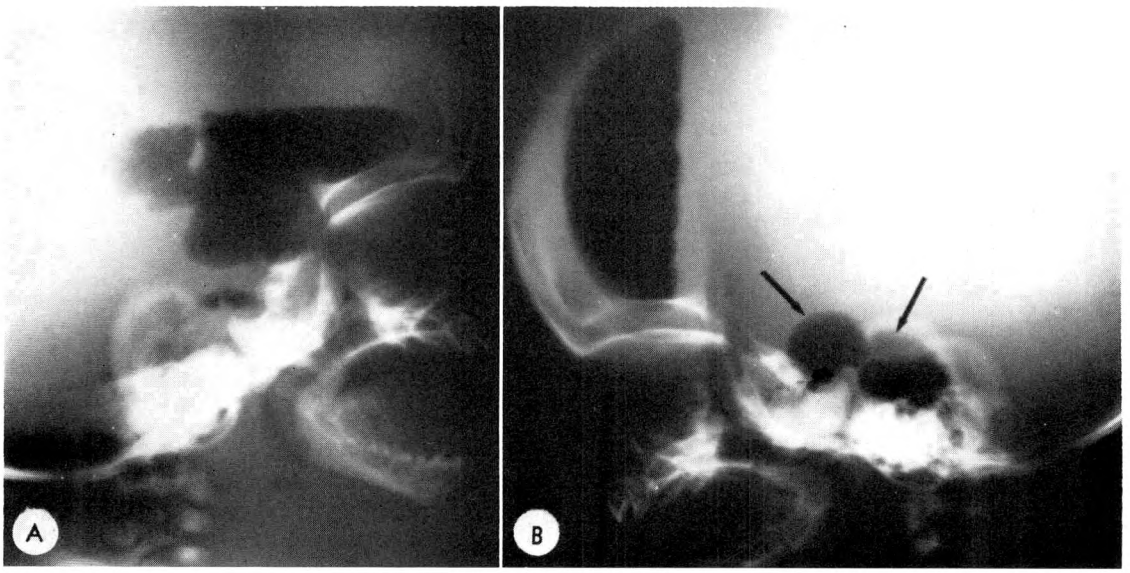


FIG. 14. Case 22. (*A* and *B*) Note the advanced dilatation of the anterior end of the 3rd ventricle, also the small massa intermedia. The 3rd ventricle, despite its ballooning, is lying high above the sella, displaced by the dilated pontine and interpeduncular cisterns seen in *B* (arrows).

hydrocephalus. Scatliff and Bull[25] reported cases of secondary carcinoma in the suprasellar region indenting the anterior part of the 3rd ventricle. It is apparent that defects in the 3rd ventricle in cases of extra-ventricular hydrocephalus may in-

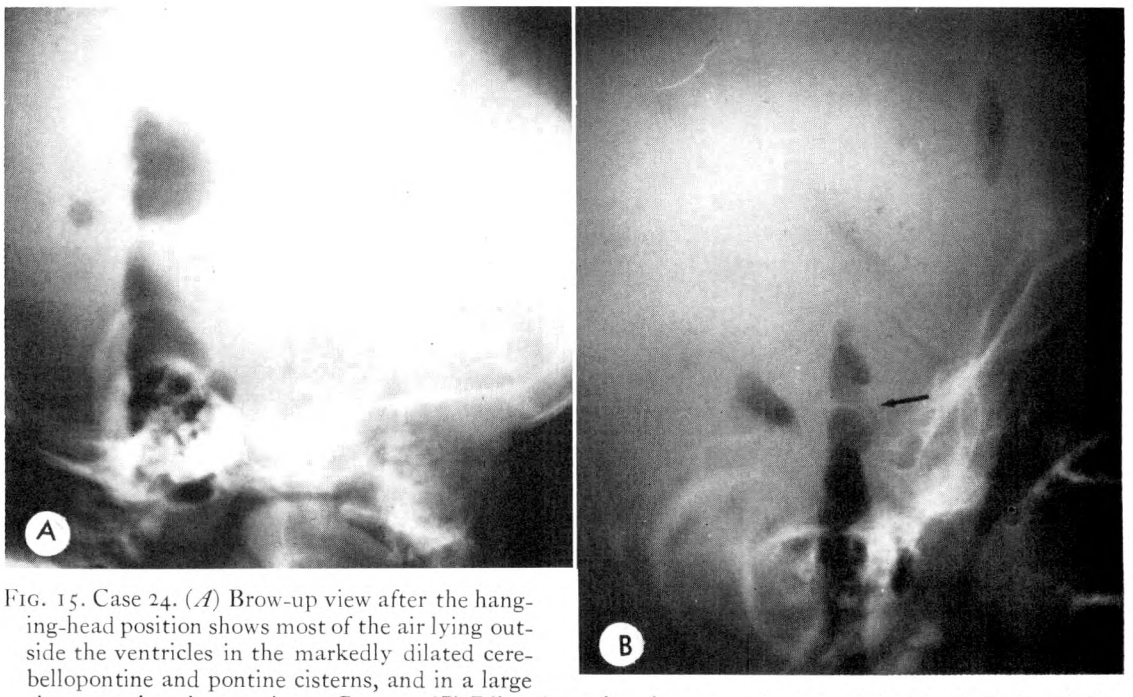


FIG. 15. Case 24. (*A*) Brow-up view after the hanging-head position shows most of the air lying outside the ventricles in the markedly dilated cerebellopontine and pontine cisterns, and in a large cisterna velum interpositum. Case 23. (*B*) Dilated pontine cistern producing a defect in the infundibular recess of the 3rd ventricle which is not dilated (arrow).

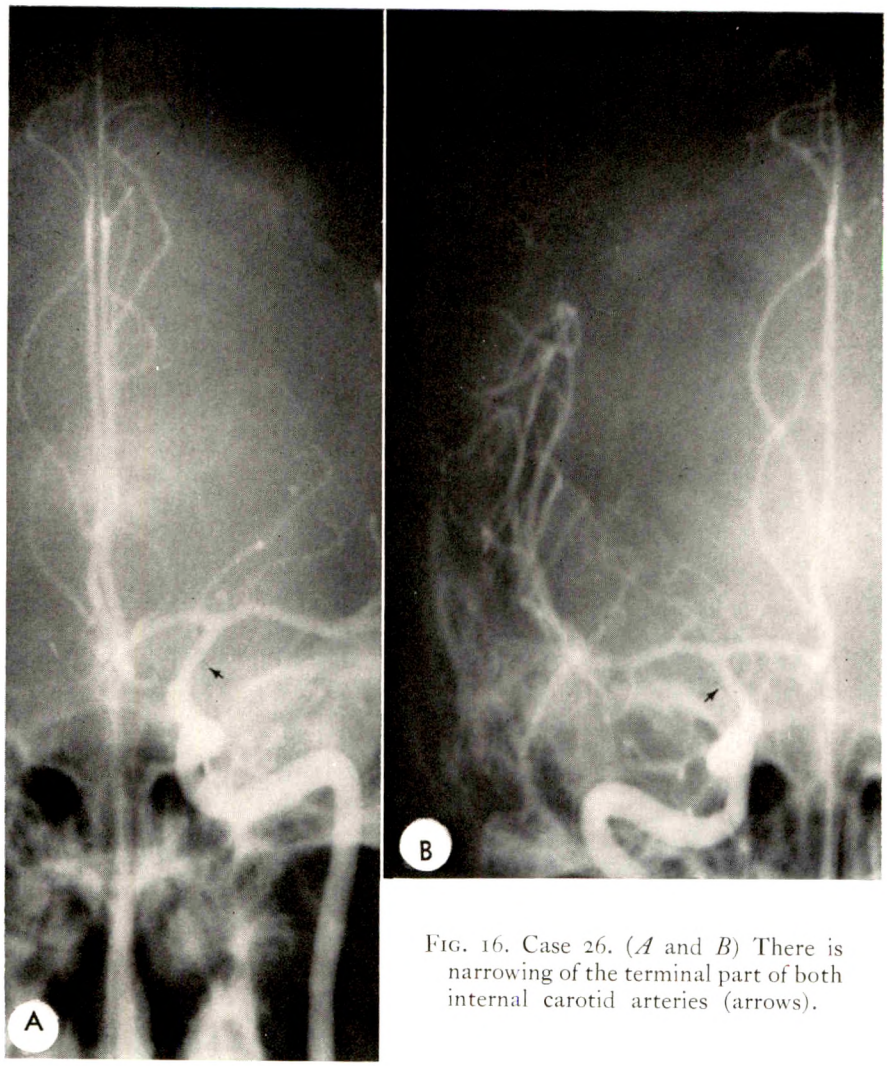


FIG. 16. Case 26. (*A* and *B*) There is narrowing of the terminal part of both internal carotid arteries (arrows).

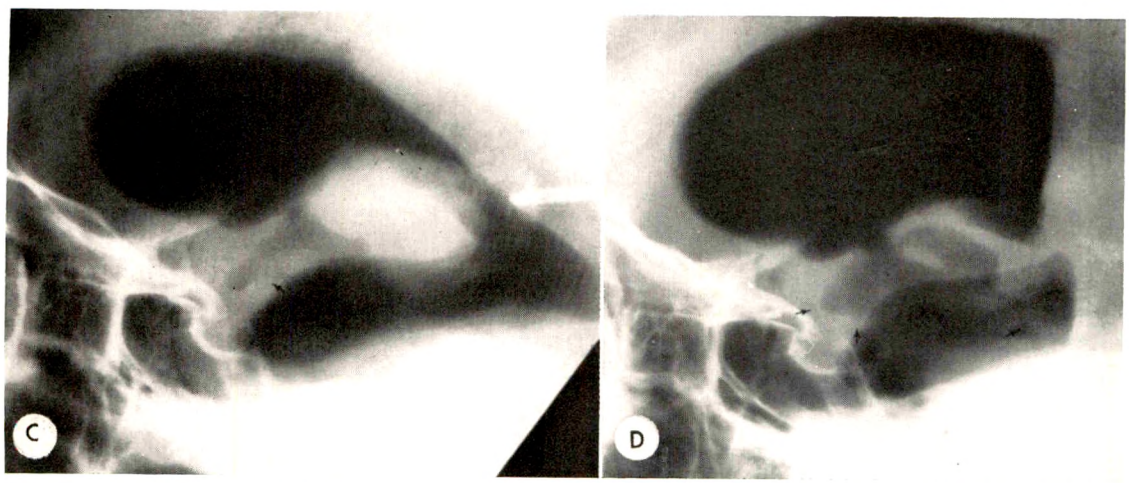


FIG. 16. (*C*) The second ventriculogram shows obliteration of the infundibular recess with a smooth defect in the floor of the 3rd ventricle. (*D*) First ventriculogram showing dilatation of the anterior end of the 3rd ventricle, particularly its optic recess. No deformity is noted in the floor of the 3rd ventricle (arrows). Some air is seen in the upper part of the aqueduct (arrow). Note also the oblong appearance of the massa intermedia with its longest diameter near the horizontal.

dicate the cause of obstruction, such as hemorrhage, inflammation, or malignant infiltrate (malignant meningitis).

(d) The massa intermedia appeared as a horizontal slit in 2 cases with hypothalamic masses. The same appearance was also seen in some cases where the lateral ventricles were markedly dilated. This may be due to pressure from below in the hypothalamus or from above by the distended lateral ventricles. We have seen the massa intermedia deformed by pressure from be-

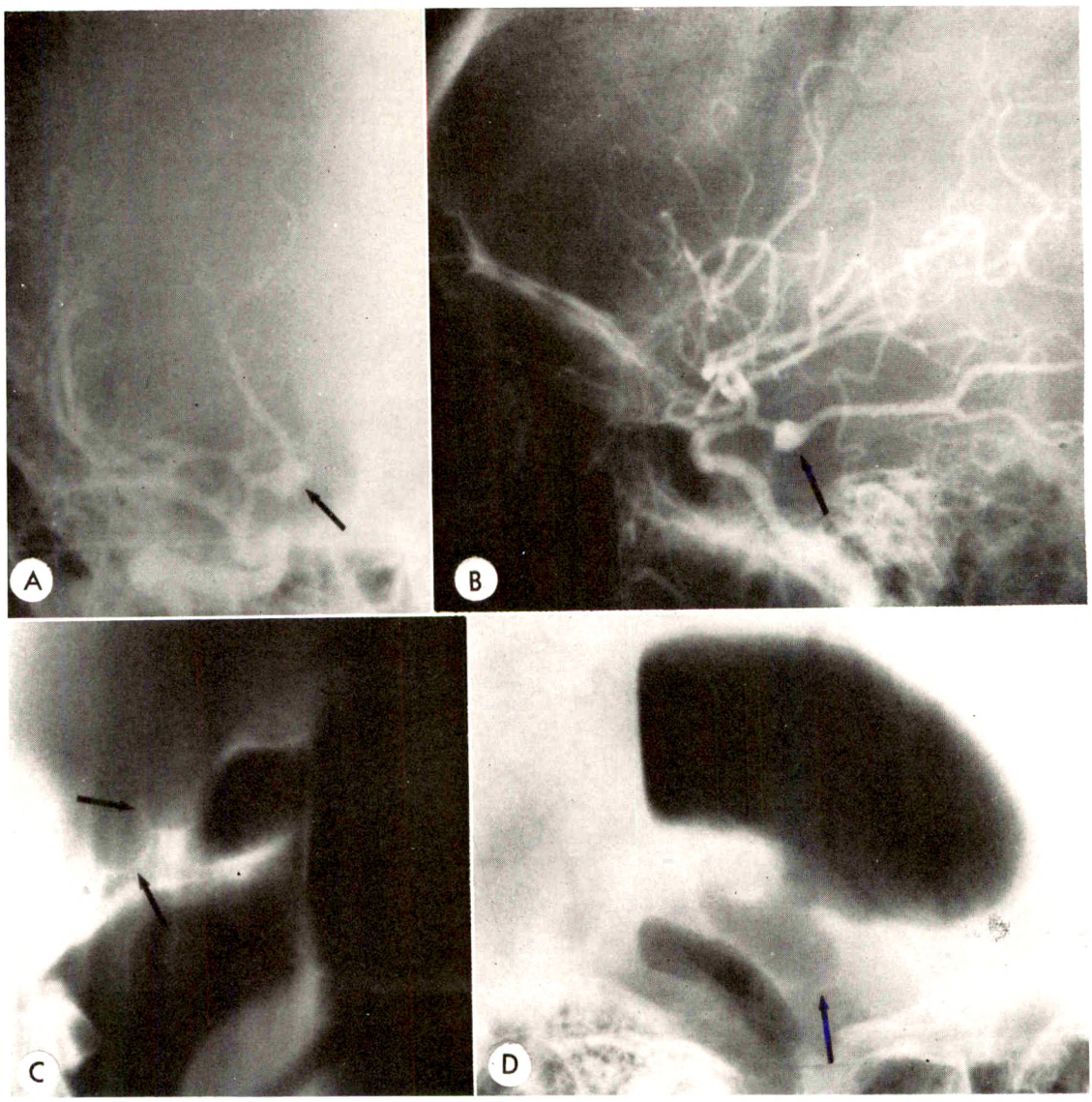


FIG. 17. Case 27. (*A* and *B*) Right carotid arteriograms (anteroposterior and lateral) showing an irregular aneurysm arising at the junction between the posterior communicating and posterior cerebral arteries (arrows). (*C*) Lateral tomogram of the sella showing erosion of the lamina dura in the anterior sellar floor, marked thinning of the dorsum sellae (upper arrow) and a well corticated defect in the upper part of the clivus, probably produced by a large aneurysmal clot and giving rise to an unusual hourglass sella (lower arrow). (*D*) The anterior end of the 3rd ventricle is dilated, its recesses cannot be identified. Despite the dilatation of the anterior end of the 3rd ventricle, it lays high above the sella turcica, probably displaced by the aneurysm. Note also the slit-like appearance of the massa intermedia with its long axis lying horizontally (arrow).

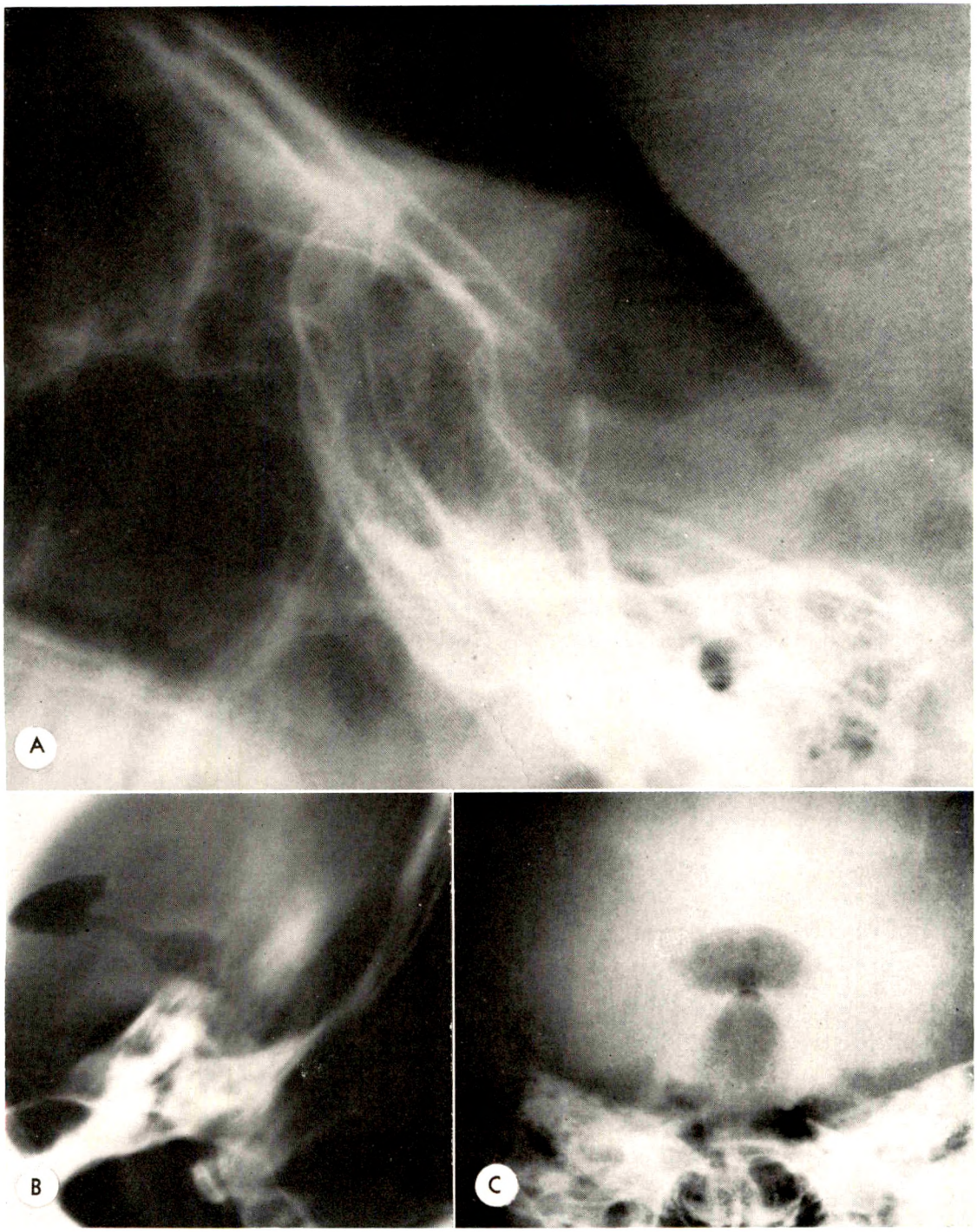


Fig. 18. Case 28. (*A*) Ballooning of the anterior end of the 3rd ventricle lying on the sella. The optic and infundibular recesses can no longer be identified. (*B*) Mild dilatation of the 4th ventricle and aqueduct. (*C*) Advanced dilatation of the 3rd ventricle in its transverse diameter.

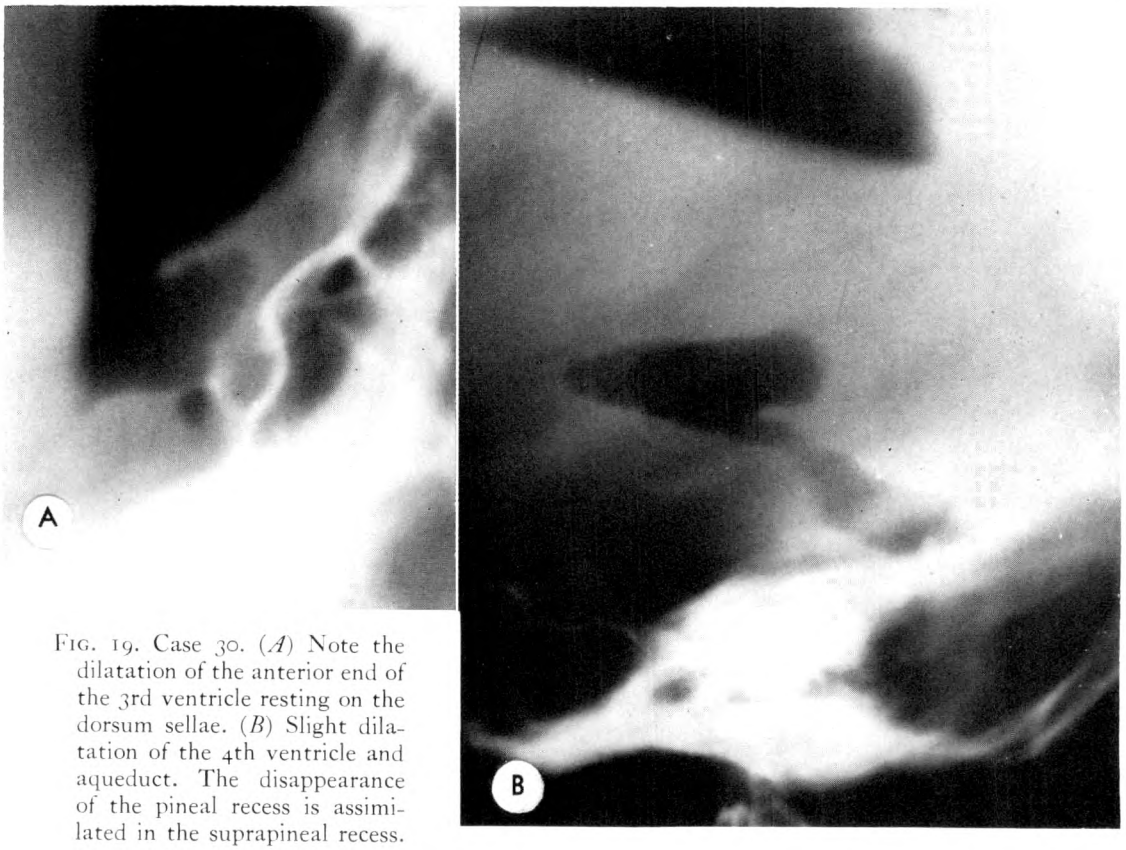


FIG. 19. Case 30. (*A*) Note the dilatation of the anterior end of the 3rd ventricle resting on the dorsum sellae. (*B*) Slight dilatation of the 4th ventricle and aqueduct. The disappearance of the pineal recess is assimilated in the suprapineal recess.

hind in some cases of large pinealomas and midline tentorial meningiomas, the massa intermedia appearing as a vertical slit (Fig. 20). In order to check the validity of the flattened appearance of the massa intermedia as a sign of hydrocephalus, 50 cases of cerebral atrophy were selected in which the 3rd ventricle was adequately shown. Seven cases showed a horizontal slit-like massa, in 2 of these the floor of the 3rd ventricle was indented by a high basilar artery. Therefore, although the slit appearance of the massa intermedia may be seen more in cases of hydrocephalus, this sign does not seem to be pathognomonic.

CONCLUSIONS AND SUMMARY

Fourteen cases of meningomyelocele with hydrocephalus and 17 cases of extraventricular hydrocephalus due to various causes are presented and the following conclusions are drawn:

1. In cerebellar dysplasia (Arnold-Chiari syndrome) the deformity of the anterior 3rd ventricle produced by an accessory transventricular connexus proved to be helpful in establishing the diagnosis, particularly in cases with complete aqueduct obstruction.

2. Dilatation of the anterior end of the 3rd ventricle points to obstruction of the cerebrospinal fluid pathways in cases of dilatation of the lateral ventricles. This sign is useful in differentiation from simple atrophy.

3. A dilated anterior 3rd ventricle, lying high above the sella in children, is usually due to dilated interpeduncular cisterns. When seen this suggests that the obstruction in the subarachnoid space has extended beyond the posterior fossa.

4. Defects in dilated 3rd ventricles may suggest the etiology of the extra-ventricular hydrocephalus (hemorrhagic, inflammatory or neoplastic meningitis).

5. The appearance of the massa inter-

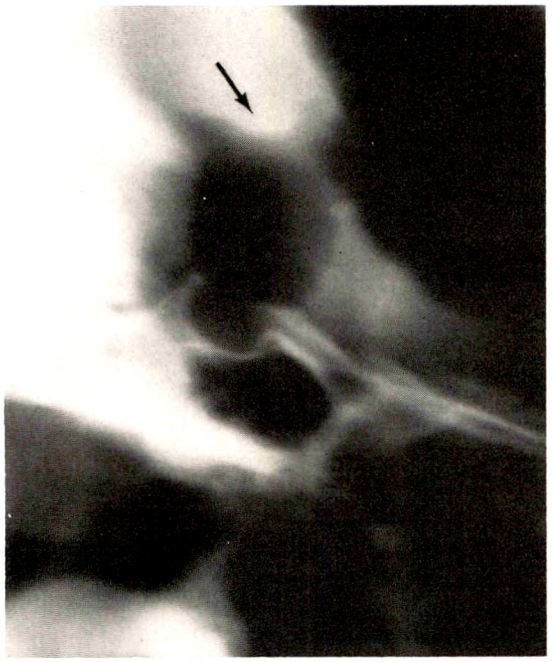


Fig. 20. A case of pinealoma. Hanging-head lateral autotomogram showing dilated end of the 3rd ventricle. Note the flattened massa intermedia with its long axis lying vertically due to pressure from behind (arrow).

media is not a reliable differential sign between cerebrospinal fluid obstruction and simple atrophy.

6. Marked dilatation of the 4th ventricle is usually associated with obstruction near the exit foramina of the 4th ventricle. If the dilated 4th ventricle is seen low at the foramen magnum, the possibility of Dandy-Walker syndrome should be considered.

7. Upward displacement of the 4th ventricle may be produced by cystic dilatation of the posterior fossa cisterns.

8. In obstructions distal to the posterior fossa, the 4th ventricle is usually normal but may show minimal dilatation.

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VOL. 106, NO. 2

LUCENT UNILATERAL SUPRATENTORIAL DERMOID CYST*

REPORT OF AN UNUSUAL CASE

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AN INTRACRANIAL dermoid cyst presenting as a unilateral lucent mass without calcification or abnormality of the cranial vault is rare. We have been able to find only 1 previously reported case in the English language literature.[8] The purpose of this communication is to present an additional case of this unusual phenomenon.

REPORT OF A CASE

A 20 year old female (Hospital No. 159299) presented at our hospital in February, 1963 after experiencing 2 grand mal seizures. She complained of bitemporal headaches worse on the left, nausea and dizziness. These symptoms subsided quickly. The neurologic examination was normal and the electroencephalogram showed diffuse slow wave activity with minimal accentuation in the left temporal area.

Roentgenograms of the skull revealed a rounded lucency measuring approximately 4 cm. in diameter situated near the floor of the left anterior fossa with no accompanying calcification. A pneumoencephalogram demonstrated a localized smooth indentation on the body of the left lateral ventricle. The anterior horn on the left side did not extend as far anteriorly as the one on the right.

Left carotid angiography revealed a 2 mm. shift of the anterior cerebral artery across the midline. The proximal branches of the middle cerebral artery were smoothly draped around the avascular lucent mass. The internal cerebral vein was not displaced. A congenital tumor close to the left caudate nucleus was suspected.

Surgical exploration was deferred and the patient was discharged on diphenylhydantoin medication.

She was readmitted in October, 1967, with complaints of faulty memory, tiredness, and headaches for the past year and of having experienced 3 more seizures since her first admission. A left facial palsy had been present for the past 3 months. A physical examination revealed no other abnormality except the left facial palsy which was thought to be a residual Bell's palsy.

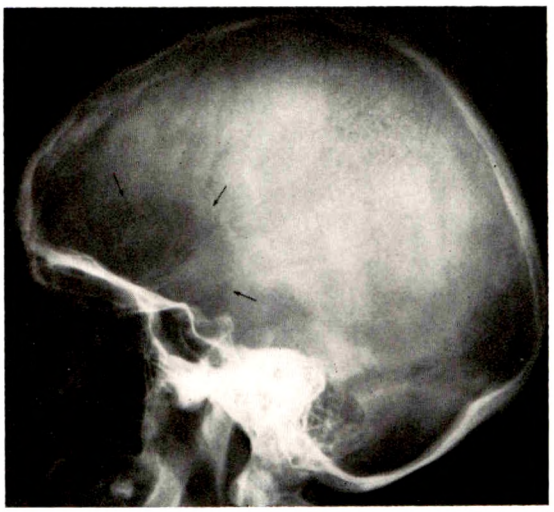


FIG. 1. Lateral roentgenogram of the skull. The 5 cm. lucency in the left anterior fossa is shown.

Skull roentgenograms and a left carotid angiogram showed the lucent mass to have increased in diameter by 1 cm. since 1963 (Fig. 1–5). Diagnostic possibilities included a lipoma or an epidermoid tumor.

A left frontal craniotomy was performed. The margin of the tumor presented along the floor of the anterior fossa and had the gross appearance of a lipoma displacing and invaginating the brain upwards. It separated readily from the brain over the majority of its surface where it had done no more than invaginate the brain tissue remaining outside the pia arachnoid. There were some loose fibrovascular adhesions superiorly towards the midline which were easily divided. Inferiorly, the

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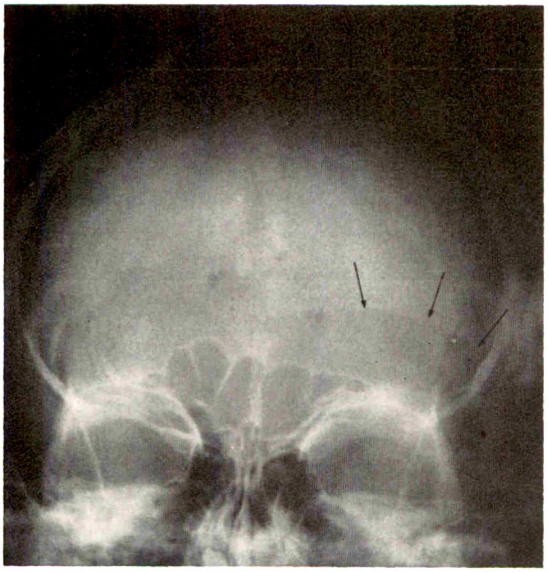


FIG. 2. On the posteroanterior roentgenogram of the skull, the superior aspect of the mass on the left is seen.

mass approximated the entire dural floor of the left anterior fossa but was not adherent at any point. As the tumor was manipulated, it became evident that it was not a lipoma but a cystic mass with a very thin encompassing membrane which ruptured during removal. It contained ceruminous material and blond hair. The entire mass came away easily. It did not approximate the sella or the parasellar structures. Continuity with brain substance was minimal, and only at the point of the thin fibrovascular connections.

The patient made an uneventful recovery and was discharged 14 days after admission.

DISCUSSION

Intracranial dermoid is an uncommon tumor. In Cushing's series of 1,936 verified brain tumors, there were 3 dermoids.[12] At the New York Neurological Institute, 2 dermoids were found in a series of about 450 verified tumors.[3] According to Rand and Reeves,[16] the incidence of dermoid and epidermoid tumors is 0.4 per cent of all intracranial growths.

Dermoid tumors are considered to be developmental anomalies. They are lined by squamous epithelium and may contain elements from any part of the dermis, including hair, sebaceous and sweat glands, teeth, nails, and skin. Development of midline dermoid tumors is thought to result from inclusion of epidermal and dermal tissues during the fusion of the medullary groove

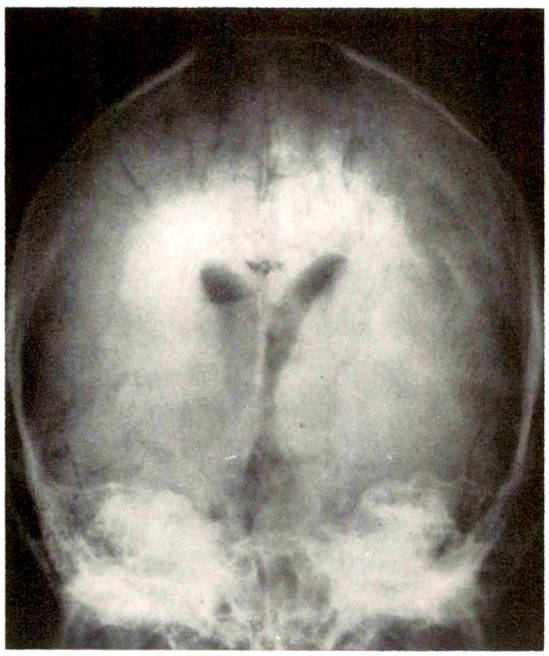


FIG. 3. The anteroposterior brow-up study of the pneumoencephalogram reveals a smooth indentation on the body of the left lateral ventricle without shift of the midline structures.

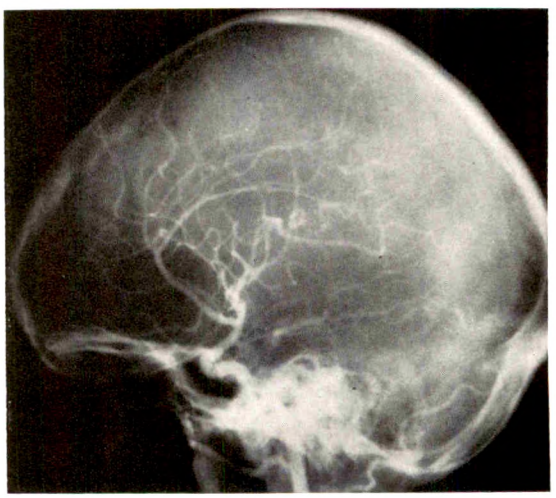


FIG. 4. Lateral projection of the left carotid angiogram during the early arterial phase. The anterior branches of the middle cerebral artery are smoothly draped around the lucent mass in the inferior aspect of the left anterior fossa.

which takes place during the third and fifth weeks of fetal life.[3] These are almost always located dorsally. Cell rests misplaced with the development of the forebrain and the developing hindbrain are thought to result in laterally placed dermoids. This occurs about the fourth and fifth weeks of fetal life. Differentiation in growth from primitive multipotential embryonic cell rests is an additional possibility.[6]

These tumors are usually encapsulated, may be soft and are usually opaque. They are yellowish or brownish in color, depending on the amount of hemosiderin within them, and contain a great deal of sebaceous material. They always contain hair and this has been considered pathognomonic of a dermoid. Histologically, they resemble skin with a fibrous outer layer containing connective tissue stroma. The latter may contain blood vessels, hair follicles, fat cells, smooth muscle cells, elastic fibers, calcium or cartilage, and sebaceous glands. There is an epithelial inner layer which varies greatly in thickness.



Fig. 5. Anteroposterior left carotid angiogram during the early arterial phase. The horizontal portion of the middle cerebral artery is elevated by the lucent mass. A 2 mm. shift of the anterior cerebral artery across the midline is demonstrated.

Patients with intracranial dermoid tumors usually have long histories. The average is about 8.5 years with the age at the onset of symptoms being approximately 22.3 years.[9] Occasionally, they present with meningitis due to rupture of the intracranial dermoid cyst.[11]

These tumors may also involve the adjacent diploic space, which results in a lytic defect of variable size with a sclerotic margin.[5,14] Infratentorial dermoid cysts are often associated with a lucent oval-shaped defect in the midline. They may occur in association with a sinus tract which extends through the cranial vault and into the soft tissues.[1,12,18]

Roentgenographically demonstrable calcification is a frequent finding in dermoid cysts. It may consist of flakes or crescentic streaks of increased density, usually in the wall of the cyst.[2,3,7,10,13,15] Teeth are occasionally demonstrated.[17]

Rarely does a dermoid cyst present as a unilateral lucent mass without accompanying calcification or lytic defects in the cranium. A lipoma of the corpus callosum is lucent, but it is usually located in the midline. The lucency of the dermoid cyst is attributed to the high fat and cholesterol content.

SUMMARY

1. A report of a case with a unilateral dermoid cyst on the floor of the left anterior fossa is presented.

2. The development, pathology and roentgen manifestations of these tumors are discussed.

3. A lucent supratentorial mass is a rare occurrence, particularly when it is not situated in the midline and not associated with calcification or cranial abnormality.

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PERFUSION I^{131} MACROAGGREGATE BRAIN SCANNING; A CLINICAL EVALUATION OF ITS DIAGNOSTIC EFFICIENCY*

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THROUGH the years constant efforts have been made to improve the technical aids to confirm the presence of intracranial lesions. Ventriculography, electroencephalography, angiography and a few clinical laboratory tests have all contributed toward the diagnosis and localization of space occupying pathologic processes of the central nervous system. Recently, radioactive tracers have added another weapon to this diagnostic armamentarium.[5,8,15,16] Even though the clinical neurologic work-up can offer valuable data, they may be misleading because of signs and symptoms produced by damage to adjacent, or even relatively distant central nervous system tissues.[13] Radiologic studies usually contribute much to the localization but even these, at times, give indefinite or noncontributory results.[1] The same may be said of electroencephalographic methods.[13] With the advent of radioisotope procedures new possibilities are being explored in the localization of intracranial expanding lesions. To date the results, as reported by various investigators, have shown considerable variation.

For all of these reasons we felt that the injection of macroaggregates labeled with I^{131} directly into the carotid artery, might be of considerable value in improving our diagnostic weapons. In Mexico this method is known as "cerebral perfusion scanning." Its success or failure would be directly based on the circulatory alterations common to a wide variety of disease conditions of the central nervous system as well as those already described in other organ systems while using the same method. We already knew that the gray matter of the central nervous system has a more or less uniform vascular irrigation.[4]

In this paper we are reporting on the results obtained by cerebral perfusion scanning in 50 patients who suffered from a wide variety of pathologic conditions. The clinical diagnosis was confirmed through the use of clinical, laboratory, radiologic, histopathologic and autopsy studies.

MATERIAL AND METHOD

Taplin *et al.*[10,11] first used I^{131} radioalbumin macroaggregates in perfusion studies in 1964. At the present time they are principally used in lung scanning. Macroaggregates are amorphous particles of irregular shape which have an average diameter of 50 micra and can be labeled with a variety of tracers. For this study we employed the Squibb and Sons product, "Albumotope," labeled with I^{131} with activity calculated to be between 800 and 1,500 μc per ml. in 1 mg. of albumin.

We used a Picker scanner with a 3 inch crystal and a 19 hole collimator. We obtained color and radiographic images.

Our series was made up of 38 male and 12 female patients with age limits from 2 to 77 years. Most of them were very ill and in 12 we eventually obtained autopsies.

The internal carotid artery, on the side corresponding to the suspected lesion, and under local or general anesthesia, is punctured with a No. 18 Cournand needle. In 80 per cent of our patients we carried out this procedure concomitantly with cerebral angiography and were thus able to control visually the placement of the needle.

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At the end of the angiographic study we inject 50 μc of I^{131} radioalbumin mixed in 5 ml. of normal saline solution. The injection is carried out slowly (20 seconds) and the needle is then immediately withdrawn. Pressure is applied over the injection site for 5 minutes in order to avoid hematoma formation. The patient is then placed on the scanning table, and tracings are obtained in the lateral and anteroposterior projections. The entire study is finished 1 hour after the introduction of radioactive material. Using the above stated dose we get a count level which varies from 5,000 to 8,000 per minute with the collimators moving at a rate of 50 cm. per minute.

The diagnoses in the patients studied in this series were as follows:

1. Cerebrovascular accident; diffuse or localized vascular insufficiency	12 cases
2. Primary supratentorial neoplasms	10 cases
3. Encephalitis	5 cases
4. Sub- or epidural hematoma	3 cases
5. Bacterial meningitis	3 cases
6. Meningitis secondary to cysticercosis	3 cases
7. Metastatic supratentorial neoplasms	2 cases
8. Brain abscess	2 cases
9. Infratentorial primary neoplasms	1 case
10. Cysticercosis within the brain	1 case
11. Vascular malformation: secondary hematoma within brain	1 case
12. Tuberculoma	1 case
13. Degenerative diseases	2 cases
14. Jackson type epilepsy	2 cases
15. Psychiatric disturbances	2 cases
Total	50 cases

RESULTS

The following considerations are of great importance in the interpretation of the cerebral perfusion scan:

a. If the needle is introduced into the common carotid artery, a considerable part of the radioactive substance will be lost to the external carotid artery. We have found that roentgenologic control is almost indispensable in the correct placement of the needle.

b. The time lapse between injection and scanning is of great importance since the macroaggregates disappear rapidly from the brain capillary bed. In inexperienced hands, this sometimes leads to false diagnoses of ischemic lesions, especially in the temporal lobe, where the macroaggregate particles tend to disappear more rapidly. We should point out here that even with the best technique there sometimes is less concentration of the radioactive material in the anterior subsylvian area.

c. "Cold" or ischemic zones are the result of an *in situ* lesion as well as direct or indirect pressure on blood vessels, produced, for example, by meningiomas found on convex or parasagittal surfaces.

d. The direct cooperation of the patient is always necessary since any movement on his part during the study introduces artifacts in the printed result.

e. The lateral view is more useful than the anteroposterior projection since, in the second, the thickness of the tissue scanned and therefore of its radioactive content is much greater. The limitations of penetration of the scanner and the general morphology of the cerebral hemisphere are also determining factors.

Of the 50 patients included in this study, in 40 (80 per cent) the procedure was considered to be effective and the result positive since the scan was found to correspond to an intracranial lesion. In 5 patients (10 per cent) we were unable to read the scan satisfactorily because in 3 cases the macroaggregates had entered the common carotid artery, in 1 case the vertebral artery and in the fifth the external carotid artery. In 5 patients (10 per cent) we considered the findings to be negative since the image obtained in the scan could not be correlated with the lesion which had been diagnosed clinically.

Twelve of our patients died during the months in which this study was being carried out and an autopsy was obtained in all of these cases. The brain lesions identified therein were found to correspond to the previously obtained scan. Microscopic studies of the brain did not reveal any pericapillary lesions which could be attributed to the intravascular injection of the microemboli of macroaggregates. In 1 of these

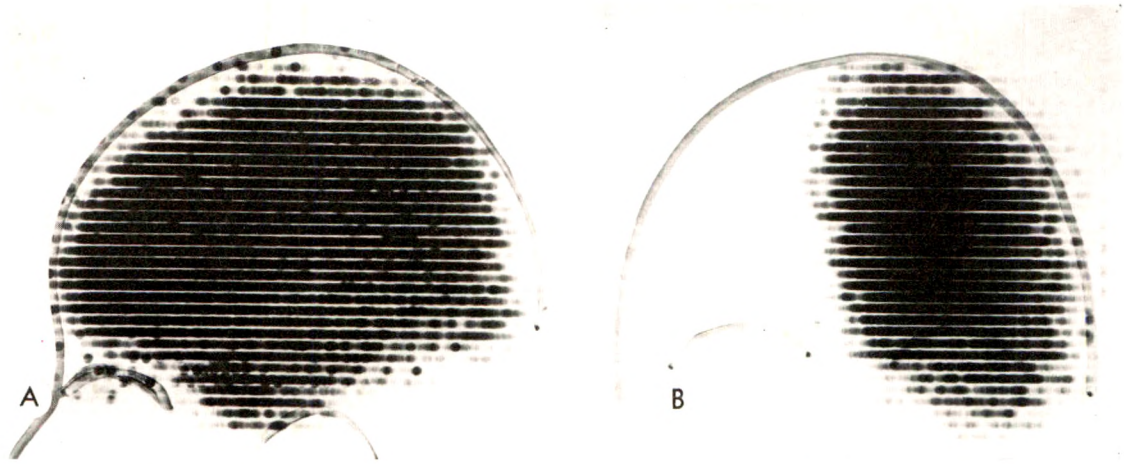


Fig. 1. (*A*) Normal macroaggregate brain scan, lateral view. (*B*) Normal macroaggregate brain scan, anteroposterior view.

cases the autopsy was done 72 hours after the brain scanning was made and no microscopic sequelae of this procedure could be identified.

In Figure 1, *A* and *B* we observe the scan image obtained in a normal person. In the temporal region there is a slightly decreased concentration of radioactive tracer. In cases of intracranial neoplastic processes as in Figures 2, *C* and *D*, 3*A*; and 4 one observes an essentially negative image in the damaged area. We believe that this is due to damage to the vascular system within the neoplastic tissue as well as to possible pressure phenomena of the tumor on neighboring blood vessels. As might also be expected, the scans produced negative images in areas of brain hemorrhage. Figure 5, *A* and *B*, is of the scan obtained in a case of a hematoma in brain substance in the right temporal lobe. Figure 6 is of a scan in a case of a large subdural hematoma over the left hemisphere. This, in turn, has been forced towards the right and downwards. In brain abscess we also identified negative areas in the scan (Fig. 7, *A* and *B*).

The over-all results in these 50 patients established that there are no characteristic scan images as far as specific lesions are concerned. The scan can inform us that there is reduced or absent vascularity in a given area in the brain, but neither its shape nor other visible features can aid us in identifying the pathologic nature of the process.

DISCUSSION

Even though perfusion scanning had been done previously in human patients,[3,4,9] the method met serious objections since it was well known that the microemboli of macroaggregates did produce obstruction of brain capillaries for short periods of time.[2,10,11] Thus, at least in theory, there existed the danger of producing micro-infarcts in the brain. On the other hand, in the course of the last 3 years we have seen several papers concerning experimental work directed towards ascertaining the real extent of the risk involved from this and other points of view. It was soon found, for example, that the procedure does not bring about an immune reaction.[12,14] The possible damage from irradiation is practically nil because of the small doses used. From the histopathologic point of view, Kennady and Taplin[2,12] using dogs, rabbits and monkeys, and Murphy *et al.*[6,7] using rabbits and rats, have studied the cerebrum and other organs without having been able to identify tissue damage and in spite of having employed very large doses. Rosenthall[9] in studies in human patients, found no pathologic changes due to the use of macroaggregates but King *et*

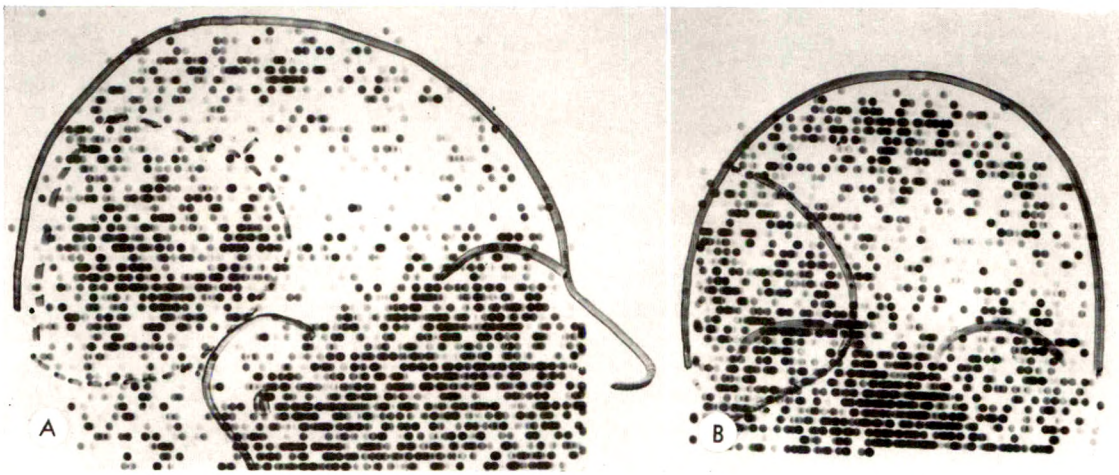


FIG. 2. (*A* and *B*) Brain scans obtained with chlormerodrin labeled with Hg^{203}. Patient with metastatic lesion in the right occipital area from lung tumor.

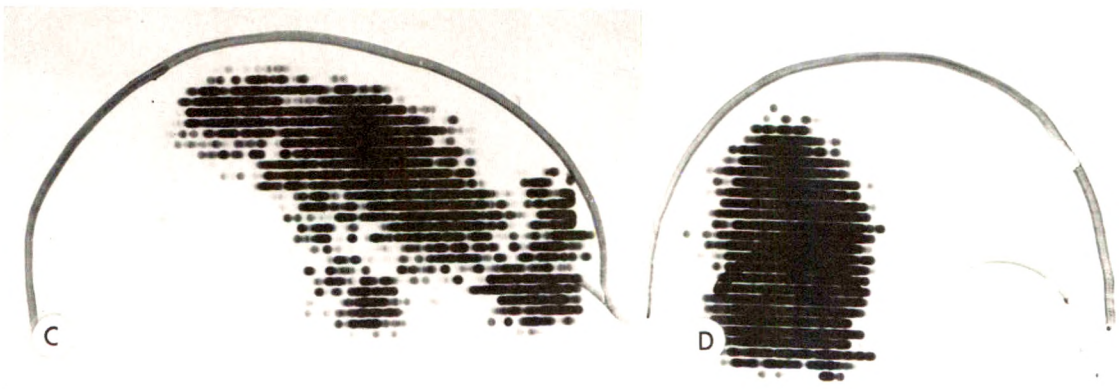


FIG. 2. (*C* and *D*) Macroaggregate brain scans of the same patient.

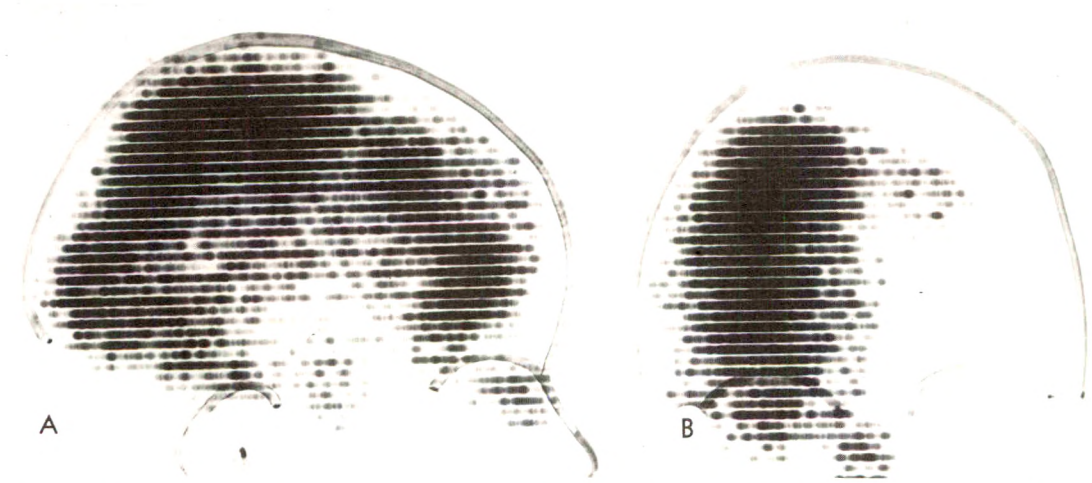


FIG. 3. (*A*) Lateral view of macroaggregate brain scan of patient with pontine glioma. An ischemic area is evident in the hypothalamic region, probably due to circulation disturbances in the circle of Willis. (*B*) Anteroposterior view. Autopsy showed pontine tumor extending towards hypothalamus.

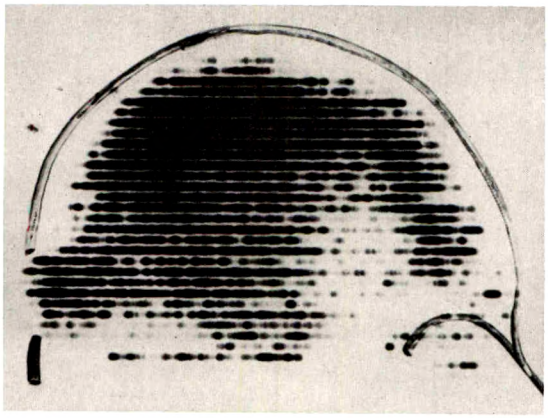


Fig. 4. Macroaggregate brain scan of patient with papillary ependimoma involving the anterior portion of the third ventricle and spreading into the frontal lobe.



Fig. 6. Macroaggregate brain scan, anteroposterior view, of patient with chronic subdural hematoma. The whole left hemisphere is displaced from the inner table.

al.[3] also working with human patients, noted transient clinical patterns suggesting a possible worsening of the patient's condition. Nonetheless, they did not establish if this was due only to the injection of the macroaggregates or to some alteration brought about in brain tissue. We have not been able to identify any changes which could be attributed to the injection procedure except for some sleepiness which lasts 1–2 minutes and is seen in some patients. There are no apparent alterations in the motor or sensory pathways. Kennady and Taplin[2] in their work with monkeys emphasize the importance of the amount of albumin used. However, they did not identify any clinical or pathologic changes in spite of having carried out studies many times in the same animal and with comparatively large doses. Their maximum dose was of 0.7 mg. of albumin with an average activity of 50 microcuries. Murphy

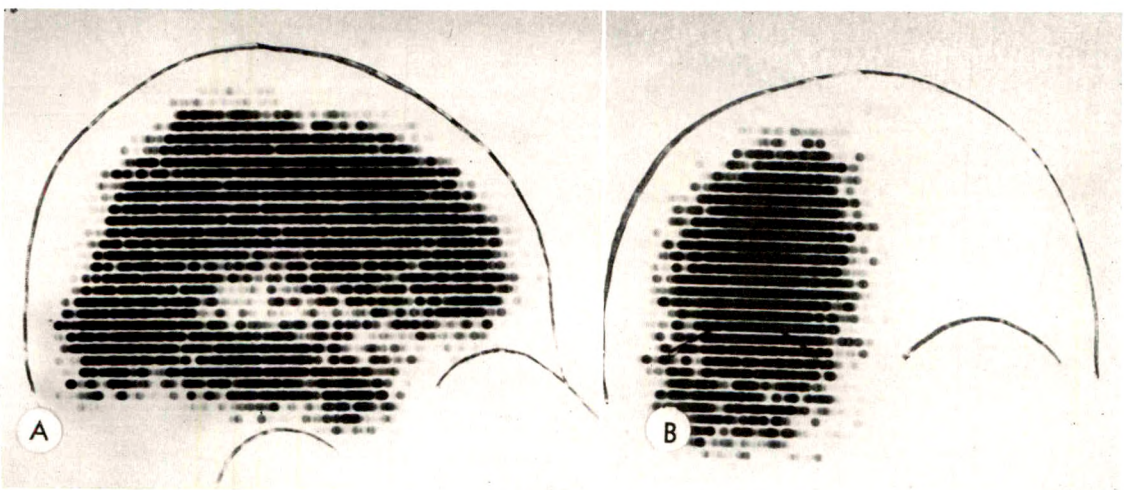


Fig. 5. (*A*) Macroaggregate brain scan, lateral view, of patient with intracerebral hematoma in the right temporal lobe area secondary to arteriovenous malformation. (*B*) Anteroposterior view shows slight ischemic area in the right temporal lobe.

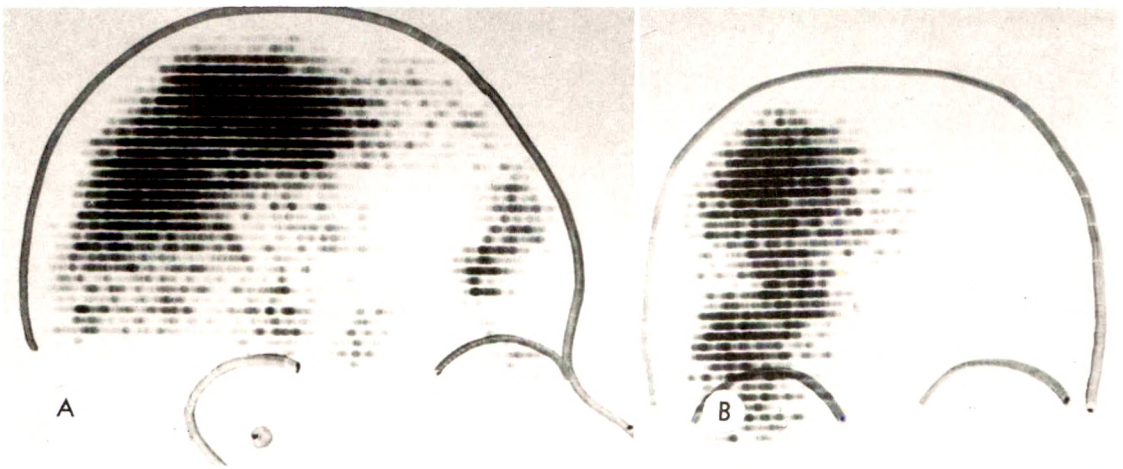


FIG. 7. (*A*) Macroaggregate brain scan, lateral view, of patient with an abscess of the right frontal lobe. The ischemic areas not continuous with the abscess are probably due to edema. (*B*) Anteroposterior view shows diffuse ischemic changes.

et al.[7] in their study of rabbit brains after macroaggregate injection concluded that there were no clinical or pathologic changes and that the use of macroaggregates in human patients was clearly justified. In their experimental animals, Murphy *et al.*[7] used macroaggregate doses which were 10 times superior (in relative values) to those used in human patients.

CONCLUSIONS

1. Cerebral perfusion scanning, if carried out with the correct technique and well correlated with the available clinical data, can make a real contribution to our diagnostic endeavor in 90 per cent of the cases.

2. In our 50 cases we were unable to identify any complications which could be attributed to the presence of the microemboli of macroaggregates in cerebral blood vessels.

3. This is not a simple procedure nor an innocuous one, since it requires a direct puncture of the internal carotid artery which may be hazardous.

4. Obviously we will need much more experience in this type of study before being able to state that it definitely has, or has not, differential diagnostic possibilities.

5. The autopsy, carried out in 12 of the patients, revealed lesions entirely compatible with those predicted in the perfusion scan both as to size and location.

6. Histologic control, carried out in other areas of the brain studied at autopsy or in surgical specimens, revealed no brain damage secondary to the presence of the radioactive macroaggregates.

SUMMARY

We have endeavored to make a clinical evaluation of perfusion scanning in a study of 50 patients with various types of intracranial pathology.

Several recent articles in the medical literature have pointed to the innocuous nature of this process insofar as the presence of the microemboli is concerned. The difference inherent is this type of brain scanning and its potential importance lie in the fact that it delineates cerebral blood flow only where this is preserved.

Under the most rigid conditions of safety, we injected 50 microcuries of the I^{131} radioactive tracer into the internal carotid artery, usually under roentgenologic control, at the end of the angiographic study. The patients were seen in the National Institute of Neurology and the injection was carried out under local or general anesthesia. The radioactive substance, diluted in 5 ml. of isotonic saline solution,

was injected on the side corresponding to the suspected lesion. Lateral and antero-posterior scannings were made.

In the body of this paper we have discussed the generally excellent correlation between the scan and clinical findings, the variety of lesions which it can localize without, however, supplying us with data which could suggest the pathologic nature of the lesion, and finally, the added proofs that the microemboli in themselves do not damage the brain tissue.

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APPEARANCE OF THE TRANSVERSE SINUSES BY BRAIN SCANNING*

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THE transverse dural sinuses are often asymmetric in appearance on both the cerebral angiogram[5,6] and the radioisotope brain scan.[2,7] A less clear delineation of the asymmetric transverse sinus on the brain scan can lead to the mistaken diagnosis of a posterior fossa lesion. The purpose of this report is to establish the incidence of asymmetry of the transverse sinus in a large number of randomly selected brain scans.

MATERIAL AND METHOD

The scans were from patients studied in the Nuclear Medicine Laboratory of the Milwaukee County General Hospital who had received approximately 200 μc per kg. of technetium 99m as pertechnetate intravenously and 200 mg. of oral potassium perchlorate to prevent the choroid plexus uptake of the pertechnetate.[1,9] Four scans in the anterior, posterior, and both lateral

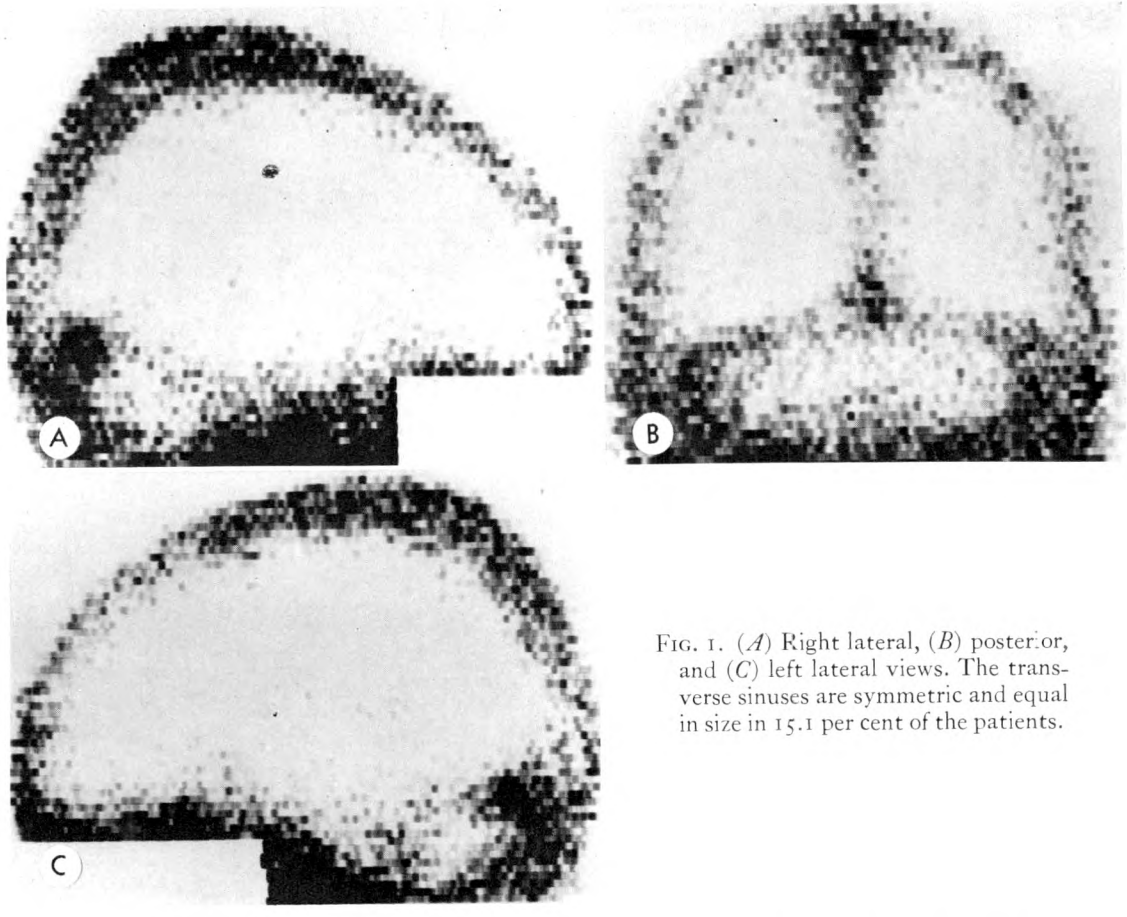


FIG. 1. (*A*) Right lateral, (*B*) posterior, and (*C*) left lateral views. The transverse sinuses are symmetric and equal in size in 15.1 per cent of the patients.

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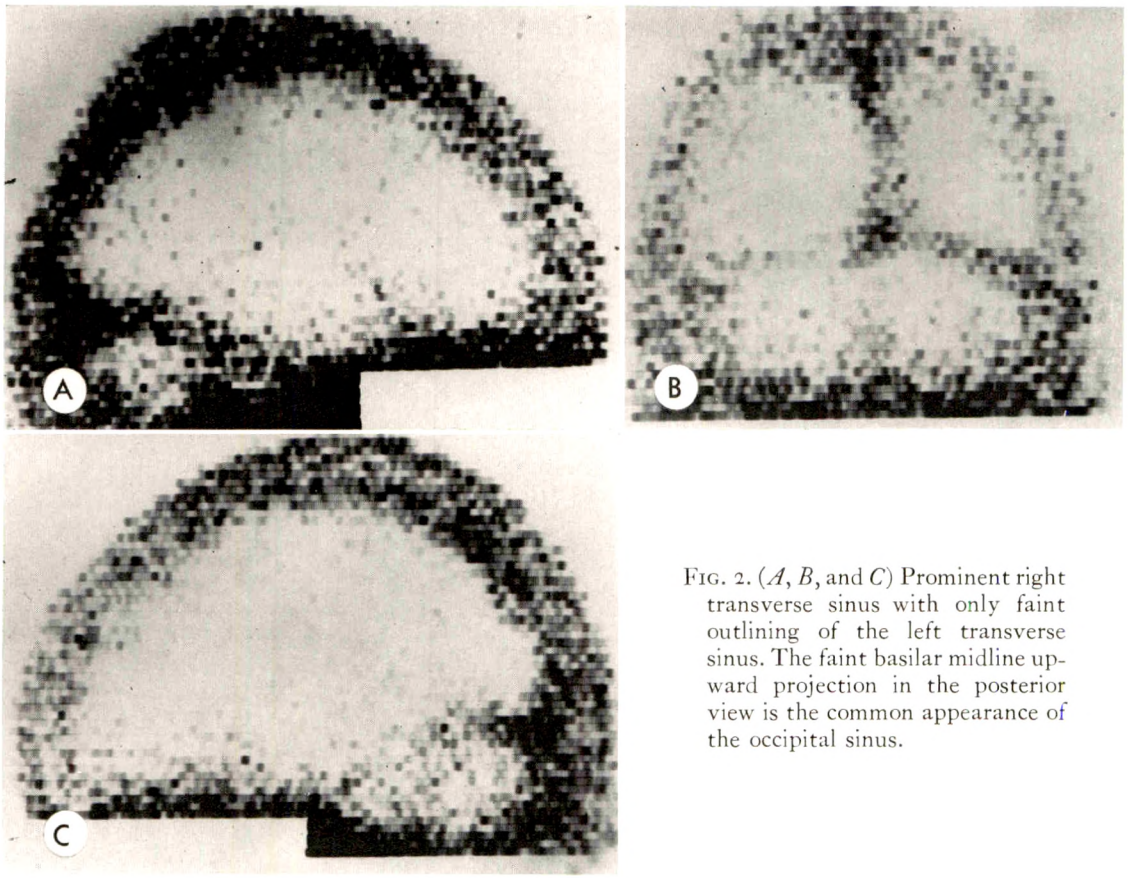


Fig. 2. (*A*, *B*, and *C*) Prominent right transverse sinus with only faint outlining of the left transverse sinus. The faint basilar midline upward projection in the posterior view is the common appearance of the occipital sinus.

positions were routinely taken. Scanning was done with a commercial 5×2 inch sodium iodide crystal rectilinear scanner equipped with a low energy, 265 hole, lead collimator focusing at a depth of 3 inches. A relatively constant distance of 2 to 4 cm. from the face of the collimator to the surface of the head was maintained in all views. To evaluate the transverse sinuses and expose the posterior fossa in the posterior view, the head was anteriorly flexed so that the chin touched or nearly touched the chest. Only the 2 lateral and the posterior scans were studied in each patient. Both the bilateral appearance and the equality or inequality in size of the transverse sinuses and the prominence of the occipital sinus were recorded.

RESULTS

The brain scans of 212 patients were selected on the basis of clear demonstration of the transverse sinuses in 2 projections at right angles to each other. Symmetric and equal sized right and left transverse sinuses were observed in 32 patients, 15.1 per cent (Fig. 1, *A*, *B* and *C*). In another 118 patients, 55.6 per cent, the right transverse sinus was prominent and was 2 to 3 times the size of the left (Fig. 2, *A*, *B* and *C*). In the remaining 62 patients, 29.3 per cent, the left transverse sinus was larger and better seen than the right, although the difference was not as great (Fig. 3, *A*, *B* and *C*). In every instance of the asymmetric predominant transverse sinus the contralateral transverse sinus was seen in one or both of the views and was fainter and occasionally smaller.

In 47 patients, 22.2 per cent, the occipital sinus, appearing as a faint, irregular midline linear density extending upward from the base of the neck toward the torcula in the posterior view, was darker and wider,

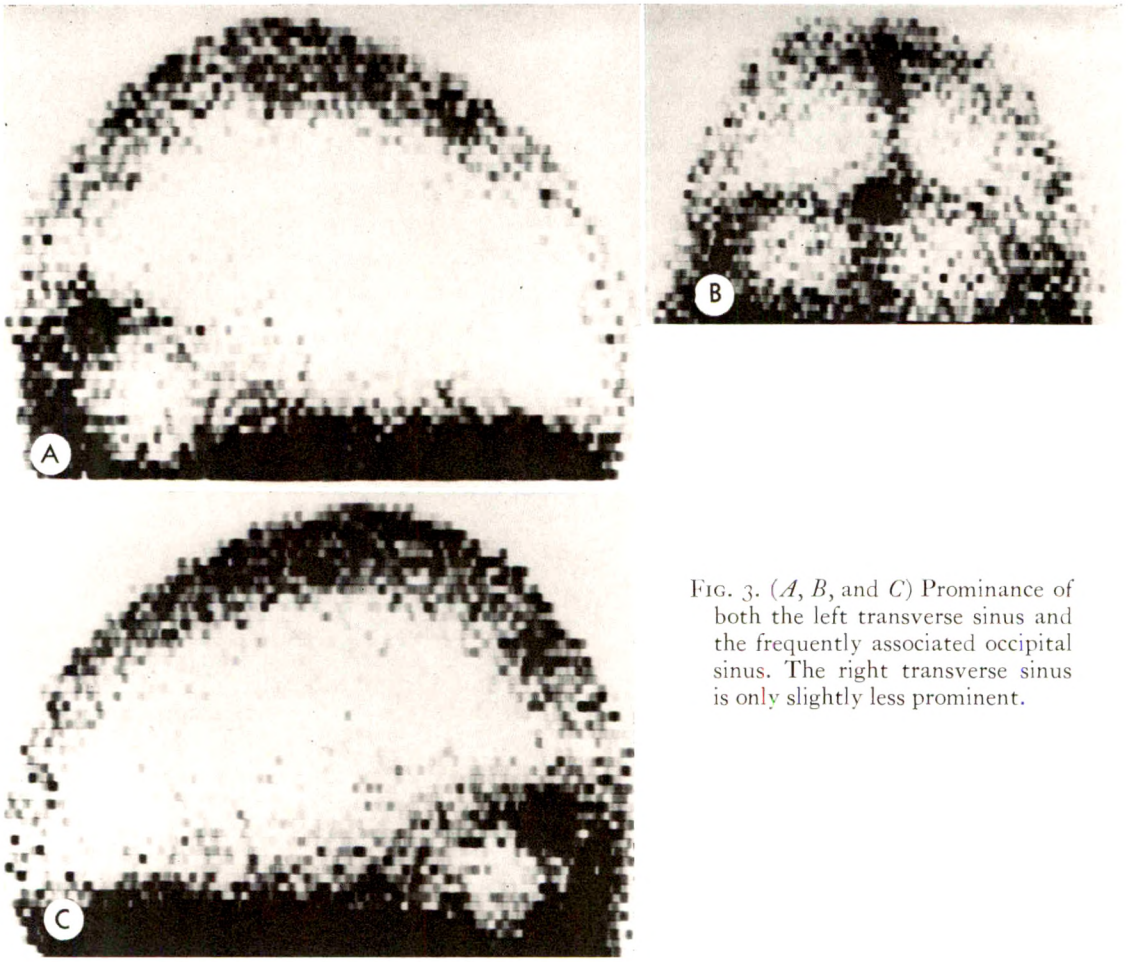


FIG. 3. (*A*, *B*, and *C*) Prominance of both the left transverse sinus and the frequently associated occipital sinus. The right transverse sinus is only slightly less prominent.

measuring greater than 1 cm. (Fig. 3*B*). This prominent occipital sinus appeared in 8 patients with the equal and symmetric transverse sinuses, in 11 patients where the right transverse sinus was dominant, and in 28 patients where the left transverse sinus was dominant.

DISCUSSION

Hollinshead states, "from the confluence of the sinuses there proceeds laterally, at the posterior border of the attachment of the tentorium to the skull, two transverse sinuses. These are frequently of unequal size; usually it is the right one that is larger, for the superior sagittal sinus often turns primarily to the right, giving off a small communication to the left transverse sinus; when this occurs, the occipital and straight sinuses usually join the left transverse sinus."[4] This representative statement is supported by the nearly 56 per cent occurrence of right transverse sinus dominance in our study.

Reports differ, however, on the frequency of transverse sinus asymmetry in cerebral angiography, with one study reporting nearly a 70 per cent incidence of equal and symmetric transverse sinuses.[3] The central streaming of the blood (laminar flow), a constant pattern of flow in the superior longitudinal and transverse sinuses, and the effect of gravity on the injected bolus of radioactive material can cause partial filling of the vessels.[6] This probably accounts for the diversity in reports,[5,6] since complete filling of vessels results when the delineating agent is uniformly mixed through-

out the vascular bed and remains so until the image of the vessels is recorded. Pertechnetate is uniformly mixed in the blood and outlines the dural sinuses on the brain scan.[7,8]

The less common appearance of a dominant left transverse sinus was frequently associated with the larger than normal occipital sinus. The similarity of the large occipital sinus to a cerebellar vermis lesion[7] may, in certain instances, be differentiated by its relationship to the dominant left transverse sinus.

False positive lesions can be suspected with the asymmetric transverse sinus if the posterior fossa is obscured by poor positioning. This results from underflexion of the head. Only when the torcula is centrally positioned in the posterior view is the scan spatially oriented and the dural sinuses are well resolved. This is assured if the head is maintained in an anteroflexed position.

A radiopharmaceutical that decays more rapidly and is cleared from the blood more rapidly than pertechnetate would eliminate the need to identify the vascular structures on the brain scan. The popularity of pertechnetate as a brain-scanning agent makes clear delineation of the vessels essential for proper interpretation.

SUMMARY

The transverse sinuses were studied on the pertechnetate brain scans of 212 patients. The symmetry or asymmetry of the transverse sinuses was determined in the posterior and lateral views.

The sinuses were equal and symmetric in 15.1 per cent. A prominent right transverse sinus was found in 55.6 per cent, and a prominent left transverse sinus was found in 29.3 per cent. In 22.2 per cent of the total number of scans, the usually barely seen occipital sinus was very prominent and dense. The largest number, 28 studies, of extra large occipital sinuses drained into the prominent left transverse sinus.

Central positioning of the torcula on the posterior scan is essential for adequate resolution of the transverse sinuses.

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THE DIAGNOSIS OF DANDY-WALKER CYST BY BRAIN SCANNING*

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THE neuroradiologic findings associated with the presence of a Dandy-Walker cyst are pathognomonic.[4] These findings relate to the cystic dilatation of the fourth ventricle which accompanies atresia of the foramen of Magendie, and, on occasion, atresia of the foramen of Luschka.

The roentgen findings consist of: (1) elevation of the torcular Herophili; and (2) high position of the lateral sinuses. For a more thorough discussion of the roentgen features of Dandy-Walker cysts, the reader is referred to the comprehensive article published by Juhl and Wesenberg.[2]

The value of the brain scan in detecting and localizing cranial lesions has been amply demonstrated.[1] A recent report illustrates the value of brain scanning in the diagnosis of intracranial cysts since they distort the normal anatomy and exhibit decreased isotopic activity.[3]

The torcular Herophili and lateral sinuses are not visualized on skull roentgenograms before the age of 1 year, and are seen in only approximately 50 per cent of patients between the ages of 1 and 2 years.[2] Brain scanning, with its lack of morbidity and mortality, constitutes an easy method for visualizing these structures.

REPORT OF A CASE

An 8 month old infant was referred to the Indiana University Medical Center because of retarded development since birth accompanied by a right upper extremity weakness. The mother's pregnancy was uncomplicated and at birth the infant weighed 7 pounds.

The infant was described as being "floppy" since birth, unable to sit up or roll over, and having a minimal degree of head control. Feeding had not been a problem.

Physical examination showed an occipitofrontal circumference of 48 cm., widening of the anterior fontanelle and slight bulging of the right forehead. A central corneal opacity was present in the left eye. Although the infant responded to painful stimuli, he appeared somewhat lethargic and unable to support his head which he held to the right. The right arm was in a flexed position and the patient demonstrated no use of this extremity. There was a facial weakness. The muscle stretch reflexes were equal bilaterally, and bilateral Babinski signs were present. Transillumination of the head revealed a large cystic area in the left frontoparietal region.

At the time of an out-patient visit, brain scanning was done. The scans (Fig. 1, *A–E*) revealed a shift of the sagittal sinus to the right with decreased activity in the left hemisphere. There was marked elevation of the torcular Herophili and lateral sinuses associated with decreased activity in the posterior fossa. This was believed to represent the presence of a cyst in both the posterior fossa and the left cerebral hemisphere.

Subsequently, the patient was admitted to the hospital for further diagnostic work-up and possible treatment. An attempt at pneumoencephalography failed to demonstrate air in the ventricles, although air did enter the basilar cisterns and could be visualized over the cerebral convexities. Ventriculography performed through the right side of the anterior fontanelle demonstrated a dilated right ventricle, an even larger left ventricle (Fig. 2*A*) and a massively dilated fourth ventricle with pronounced elevation of the tentorium cerebelli (Fig. 2*B*). The lateral ventriculogram also demonstrated a column of air present in the upper cervical spinal canal (Fig. 2*B*). On the basis of the scans and ventriculograms a diagnosis of Dandy-Walker cyst was made.

DISCUSSION

Brain scanning provides an easy method for visualizing some of the normal intra-

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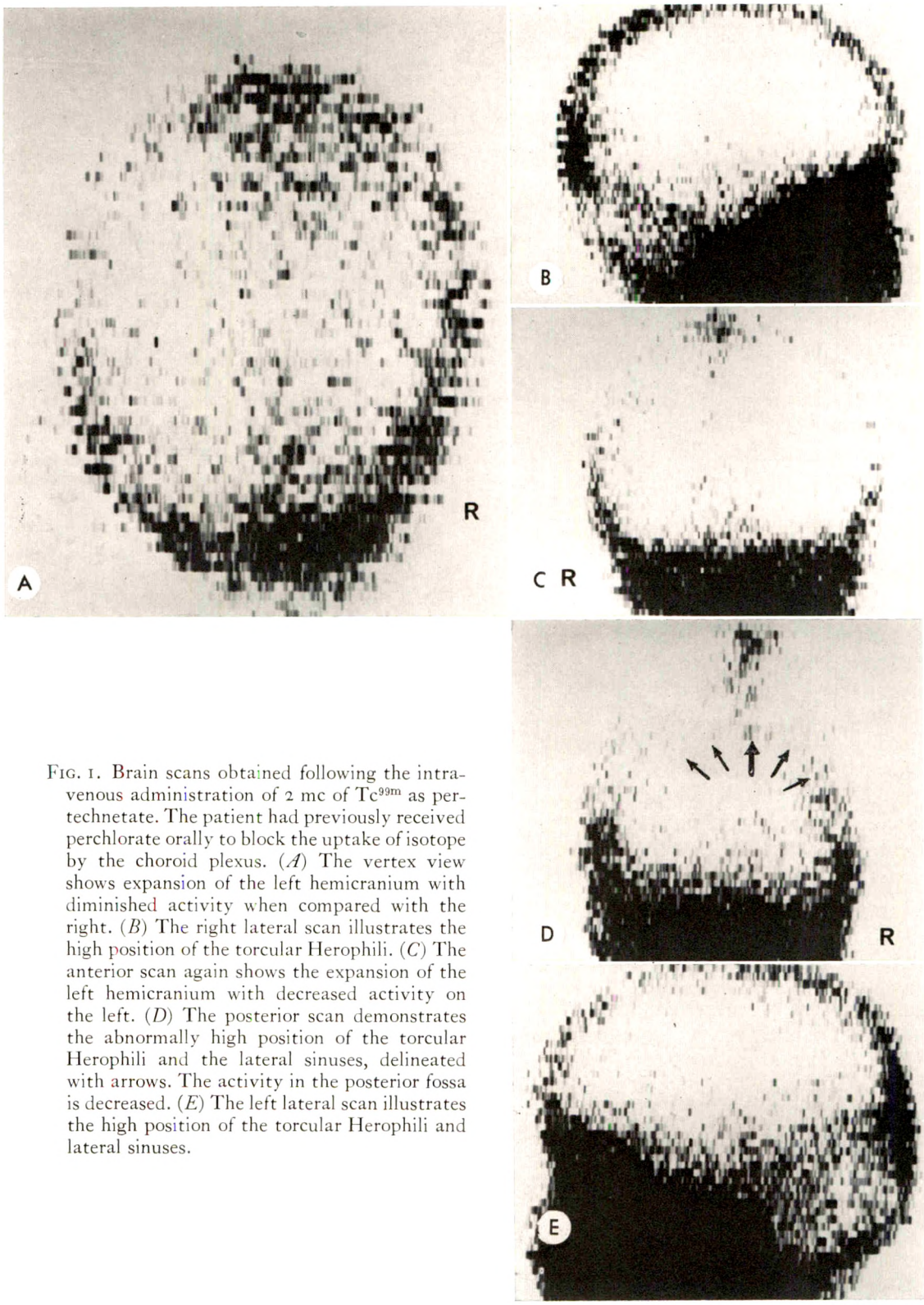


FIG. 1. Brain scans obtained following the intravenous administration of 2 mc of Tc^{99m} as pertechnetate. The patient had previously received perchlorate orally to block the uptake of isotope by the choroid plexus. (*A*) The vertex view shows expansion of the left hemicranium with diminished activity when compared with the right. (*B*) The right lateral scan illustrates the high position of the torcular Herophili. (*C*) The anterior scan again shows the expansion of the left hemicranium with decreased activity on the left. (*D*) The posterior scan demonstrates the abnormally high position of the torcular Herophili and the lateral sinuses, delineated with arrows. The activity in the posterior fossa is decreased. (*E*) The left lateral scan illustrates the high position of the torcular Herophili and lateral sinuses.

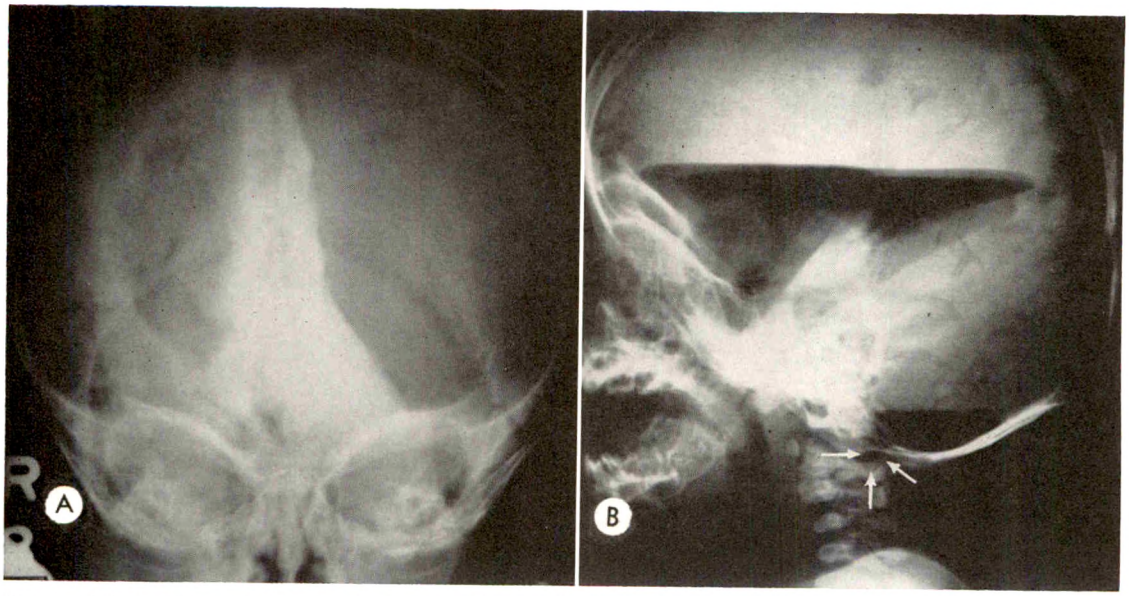


FIG. 2. (*A*) Anteroposterior ventriculogram shows thinning of the cranial vault and enlargement of both lateral ventricles, more marked on the left. (*B*) The lateral ventriculogram, with the patient inverted, demonstrates the high position of the tentorium cerebelli and air in the enlarged fourth ventricle. Arrows delineate protrusion of the cyst into the spinal canal. Thinning of the squamosal portion of the occipital bone is present.

cranial structures. In reviewing the scans of children with hydrocephalus we have found that the lateral sinuses appear relatively low in position. We have found few exceptions to this finding: in one instance the patient had cystic dilatation of the cisterna magna without evidence of arachnoiditis, and the other exception is the case reported.

In the latter case the brain scan revealed findings suggestive of a Dandy-Walker cyst with accompanying asymmetric cystic dilatation of the lateral ventricles. While the skull roentgenograms of this patient did not show the torcular Herophili and lateral sinuses, these structures were readily visualized on the brain scan, thus illustrating the value of brain scanning as an aid in the diagnosis of a Dandy-Walker cyst.

SUMMARY

A case of Dandy-Walker cyst is reported which demonstrates that it is possible to suggest the diagnosis from the brain scan. Elevation of the torcular Herophili and lateral sinuses are characteristic features of a Dandy-Walker cyst.

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THE VERTEX VIEW IN ROUTINE BRAIN SCANNING*

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THE use of the vertex view in brain scanning has been limited and it is generally not employed as a routine brain scanning projection. The ease of its performance and its ability to visualize both cerebral hemispheres in their entirety are not generally appreciated. We have, therefore, examined 638 consecutive pertechnetate brain scans in which the vertex view was routinely used in addition to the conventional projections: the anterior, the posterior and the lateral views. In the 139 cases showing an abnormality, we examined each view separately for the abnormality and compared it to the other views. The vertex view detected the highest percentage of abnormalities of all the views and is recommended as a routine view in all brain scanning procedures.

METHOD

Each patient studied received between 150 and 200 μc/kg. of technetium 99m pertechnetate intravenously. After the first 9 studies, atropine sulfate (1.0 mg. per adult patient) was administered intravenously with the pertechnetate in all but 18 of the remaining patients to reduce the uptake of the pertechnetate by the nasal and oral mucosa and by the salivary glands.[2] Two of the 18 patients received a ganglionic blocker (Arfonad) during the scanning procedure to evaluate its effect on mucosal and salivary gland uptake, which was suppressed. In more than 400 patients, 200 mg. of potassium perchlorate was administered orally 20 to 30 minutes before the pertechnetate was injected to suppress pertechnetate uptake by the choroid plexus.[1,7]

Scanning was performed with 1 of 3 rectilinear scanners: a dual 5×2 inch sodium iodide crystal scanner equipped with paired, 1,045 multiholed lead collimators; a single 5×2 inch sodium iodide crystal scanner equipped with a 256 multiholed lead collimator; or a 3×2 inch sodium iodide crystal scanner equipped with a 73 multiholed lead collimator. Each collimator focussed at a depth of 3 inches with a quarter inch radius of resolution. Counts ranged between 15 and 30×10^3 counts per minute with a pulse height analyzer baseline setting of 135 kev. and an 80 kev. window.

The vertex view was obtained first, starting within 15 to 20 minutes of the pertechnetate injection. This view was accomplished by placing the patient prone on the scanning table with the neck hyperextended, the orbitomeatal line of the head parallel to the detector face and tabletop, the head immobilized with head clamps, and the neck and shoulders covered with a lead apron.[2] The average scanning speed was 100 cm./min., and each view was completed in approximately 10 minutes.

The anterior and lateral views were completed in the usual manner. Improvement of the posterior view was obtained when care was taken to hyperflex the neck anteriorly so that the orbitomeatal line was perpendicular to the detector face and the tabletop. This elevated the transverse sinuses and centered the torcula on the scan, clearly exposing the posterior fossa (Fig. 1, *A* and *B*).[3,6]

RESULTS

Six hundred and thirty-eight studies were performed on 630 patients. Scans were repeated in 6 patients once and in 1 patient twice. Four studies were technically poor but 2 of them were repeated. A total of 139

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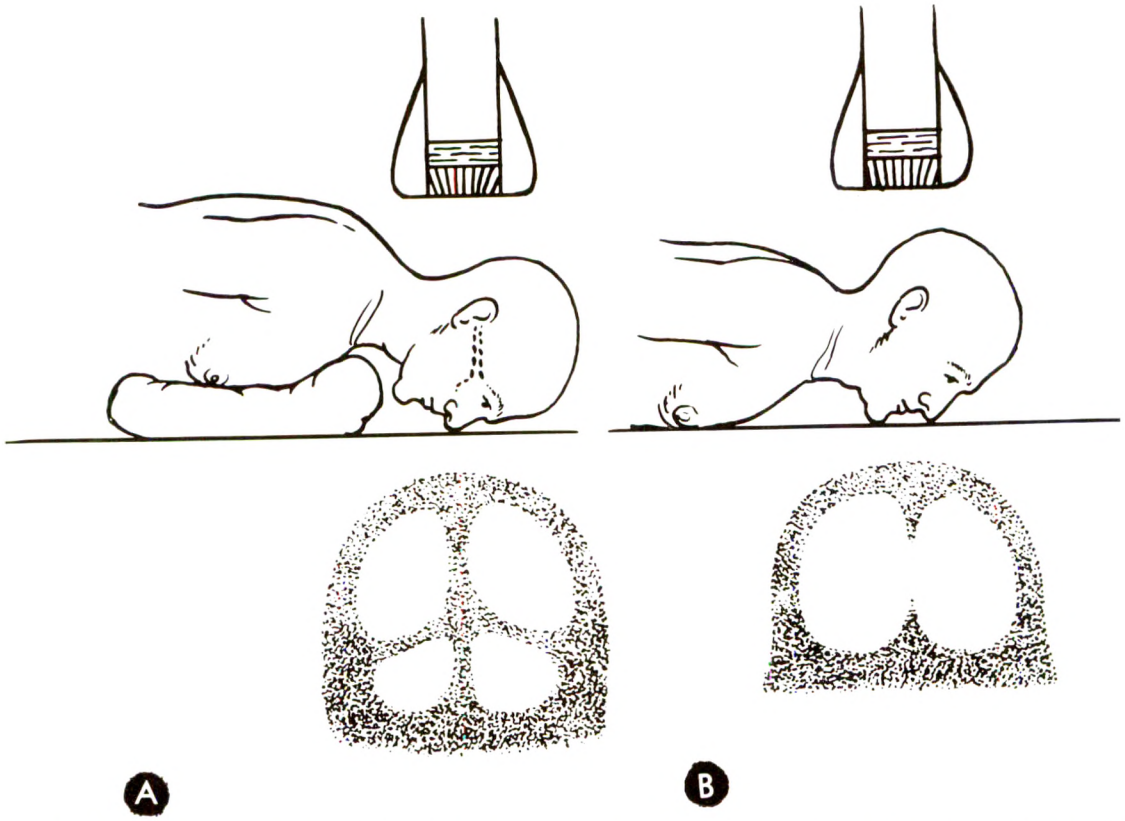


Fig. 1. Posterior view. (*A*) The head is tilted forward so that the orbitomeatal line is perpendicular to the detector surface and the tabletop. This centers the torcula and clearly exposes the posterior fossa. (*B*) The posterior fossa is not visualized when care is not taken to flex the head.

abnormal scans were diagnosed from the 638 studies. A lesion was called "positive" only when it appeared on 2 or more scans and "suspicious" when the abnormality was demonstrable on only 1 scan. Eleven patients had suspicious scan abnormalities resulting from improper positioning and rotation of the head during scanning. In several of the earlier cases before atropine was administered, excessive nasal and oral activity obscured the frontal region in the vertex view.[2]

Vertex and lateral scans were taken on all 139 abnormal cases, but only 121 cases had anterior scans and 82 had posterior scans. The lesions were demonstrable on 125 vertex scans (89.9 per cent), 58 right lateral scans (41.7 per cent), 83 left lateral scans (59.7 per cent), 84 anterior scans (69.4 per cent) and 67 posterior scans (81.7 per cent) (Table 1).

Of the 18 anterior scans that were not taken, no more than 3 of the lesions may have been demonstrable because of their

Table I

Individual view detection efficiency in abnormal brain scans

	Vertex	Anterior	Posterior	Right Lateral	Left Lateral
No. of views	139	121	82	139	139
No. of abnormal views	125	84	67	58	83
Per cent detection	89.9	69.4	81.7	41.7	59.7

dense radioactivity. The posterior view was only routine when scanning with the dual detector scanner and it was used in less than half of the studies.

Both neoplastic and non-neoplastic lesions were detected on the scans and are listed in Table II. Confirmation of the lesion was made at surgery or by other clinical and laboratory means, including resolution of vascular lesions by serial brain scanning, and at necropsy. The lesions, except for 2 cystic lesions, were characterized by single or multifocal areas of increased radioactivity, and occasionally their histopathology was suggested by their uptake, shape

TABLE II

ABNORMAL BRAIN SCAN LESIONS

1. Primary brain tumors:—glioblastoma multiforme, meningioma, astrocytoma, acoustic neurinoma, medulloblastoma, craniopharyngioma
2. Metastatic brain tumors:—lung, breast, larynx, parotid, nasal antrum, ovary, lymphoma, Wilms' tumor, melanoma
3. Vascular:—infarct, intracerebral hematoma, subdural hemorrhage, arteriovenous malformation, Rendu-Osler-Weber disease
4. Cyst:—porencephalic cyst, cystic hygroma
5. Osseous:—fibrous dysplasia, osteomyelitis, hyperostosis, Paget's disease
6. Miscellaneous:—neurofibromatosis, tuberous sclerosis, subcutaneous hematoma

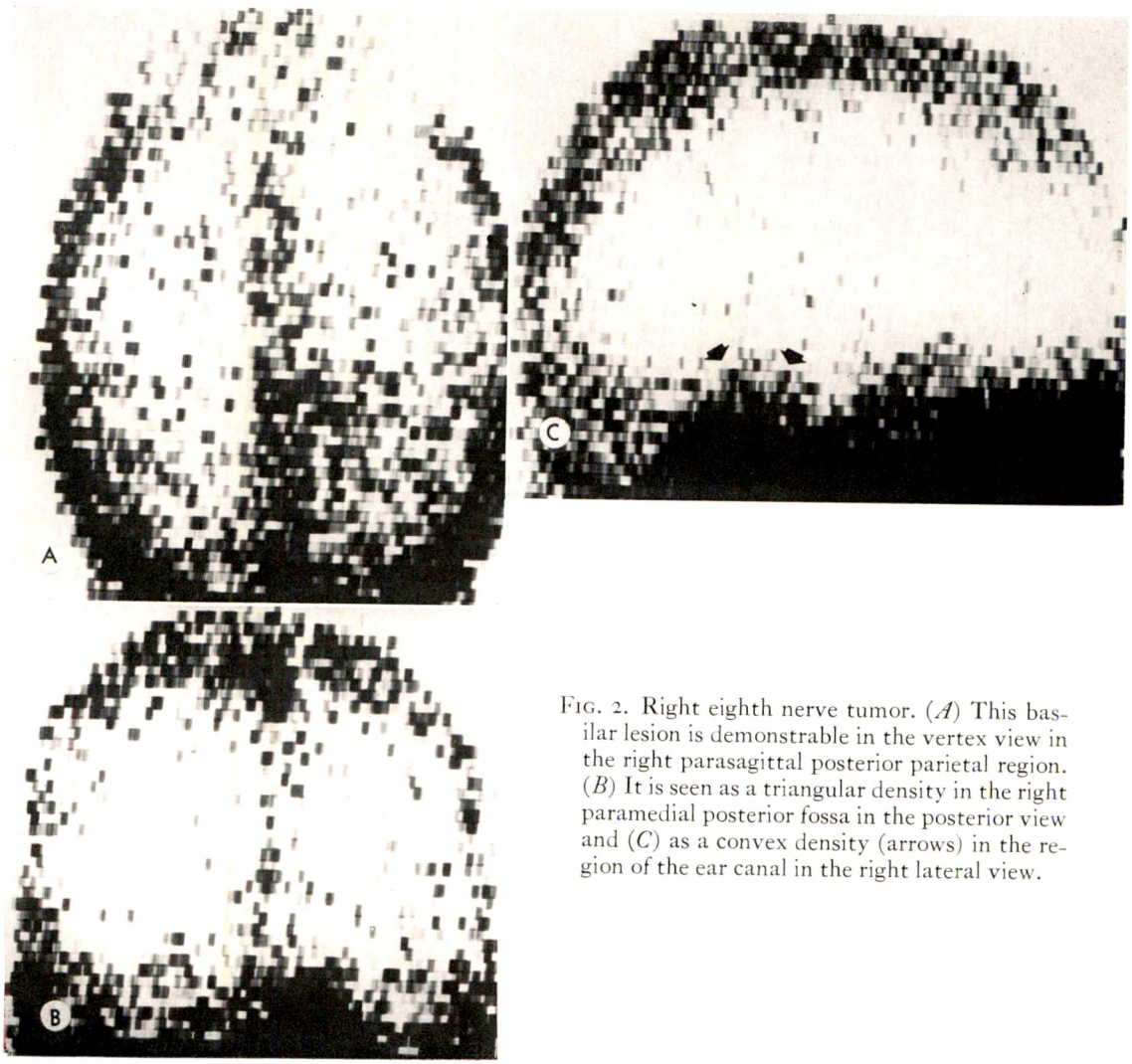


FIG. 2. Right eighth nerve tumor. (*A*) This basilar lesion is demonstrable in the vertex view in the right parasagittal posterior parietal region. (*B*) It is seen as a triangular density in the right paramedial posterior fossa in the posterior view and (*C*) as a convex density (arrows) in the region of the ear canal in the right lateral view.

and location. In 2 patients with surgically proven low grade astrocytomas, the brain scans were normal but electroencephalography and carotid arteriography demonstrated the lesions. We are unaware of other false negative scans in this group of patients.

DISCUSSION

The vertex view was reported in an earlier study as an excellent projection for demonstrating superior sagittal and parasagittal lesions.[4] We have found it advantageous, when brain scanning with pertechnetate, to administer atropine sulfate simultaneously with the pertechnetate to consistently eliminate frontal area activity in the vertex view.[2,6] As a routine view in this study the vertex view was applicable in all but a few patients with tracheostomies and severe cervical arthritis and spondylosis. When compared individually with the other views in the positive studies, the vertex view was superior to the other views, demonstrating 90 per cent of the lesions. The advantages of the vertex view re-

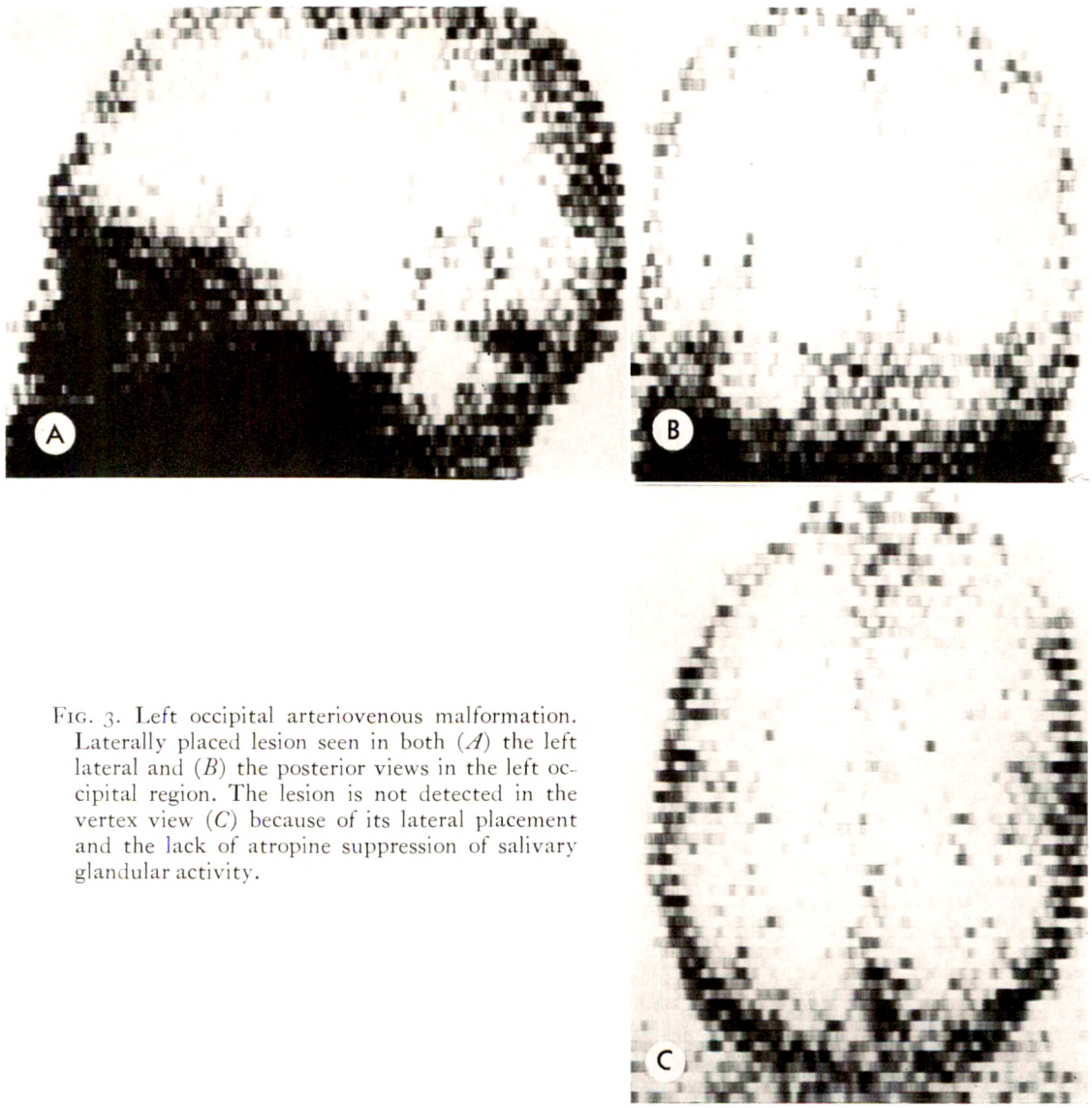


FIG. 3. Left occipital arteriovenous malformation. Laterally placed lesion seen in both (*A*) the left lateral and (*B*) the posterior views in the left occipital region. The lesion is not detected in the vertex view (*C*) because of its lateral placement and the lack of atropine suppression of salivary glandular activity.

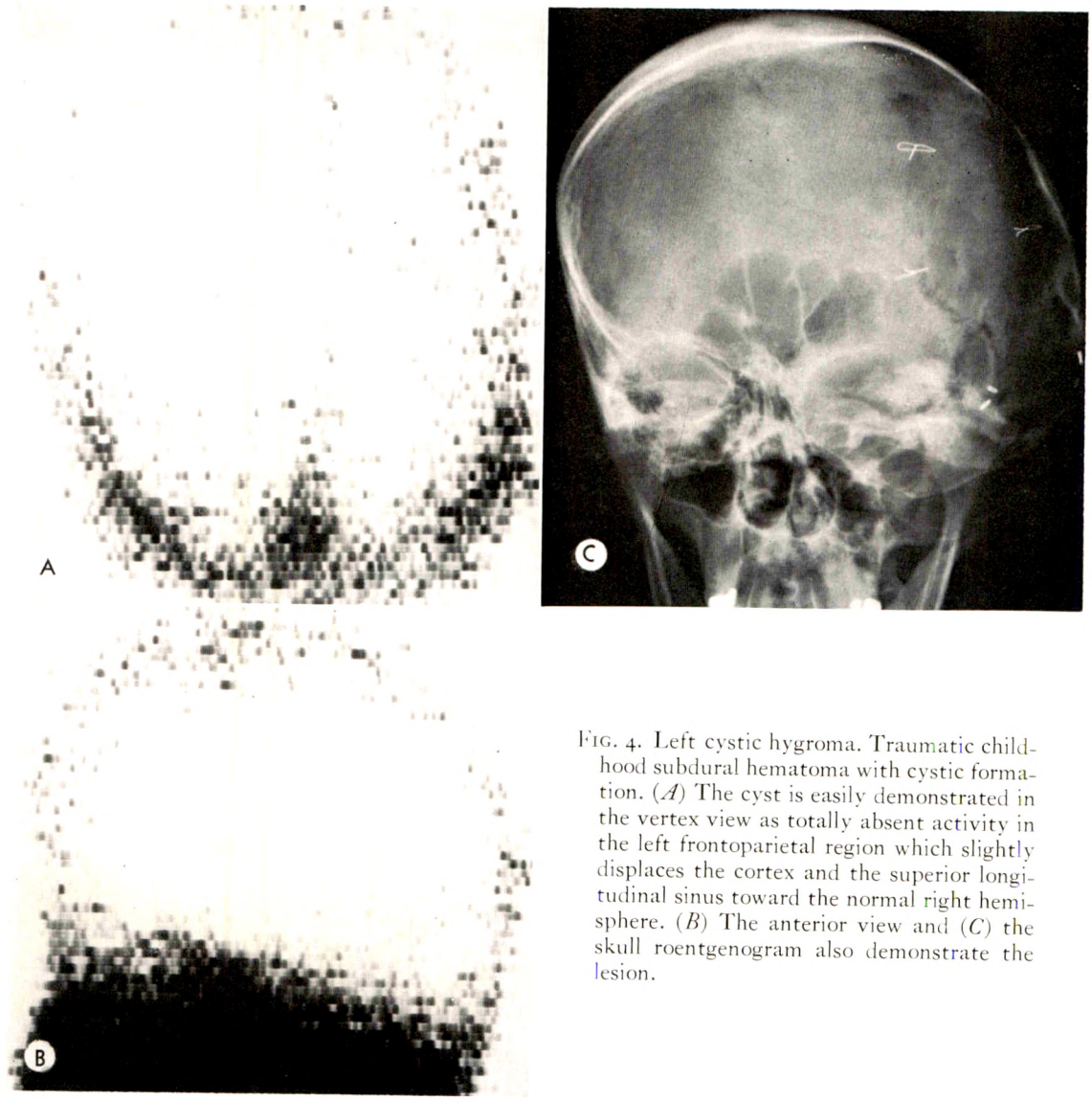


Fig. 4. Left cystic hygroma. Traumatic childhood subdural hematoma with cystic formation. (*A*) The cyst is easily demonstrated in the vertex view as totally absent activity in the left frontoparietal region which slightly displaces the cortex and the superior longitudinal sinus toward the normal right hemisphere. (*B*) The anterior view and (*C*) the skull roentgenogram also demonstrate the lesion.

sult from it being unaffected by the unilateral, the anterior or the posterior positioning of a lesion and its ability to detect basilar brain lesions (Fig. 2, *A*, *B* and *C*).

The abnormalities not detected in the vertex view resulted from the lack of atropine administration in some of the earlier studies, poor differentiation due to low contrast scans, and lesions that were laterally positioned in the head. Figure 3, *A*, *B* and *C* is an example of a vascular malformation that was not detectable in the vertex view because of its lateral position, but was visible in the posterior and lateral views.

A distinct advantage of the vertex view is its ability to detect cystic brain lesions.[5,6] In 2 patients, one with an extensive porencephalic cyst and the other with an expansive cystic hygroma, the cystic areas appeared as totally negative defects on the scans. The wide visualization of both cerebral hemispheres in the vertex view easily differentiated the cystic defect from the relatively negative activity of the normal and slightly displaced cortex of the opposite

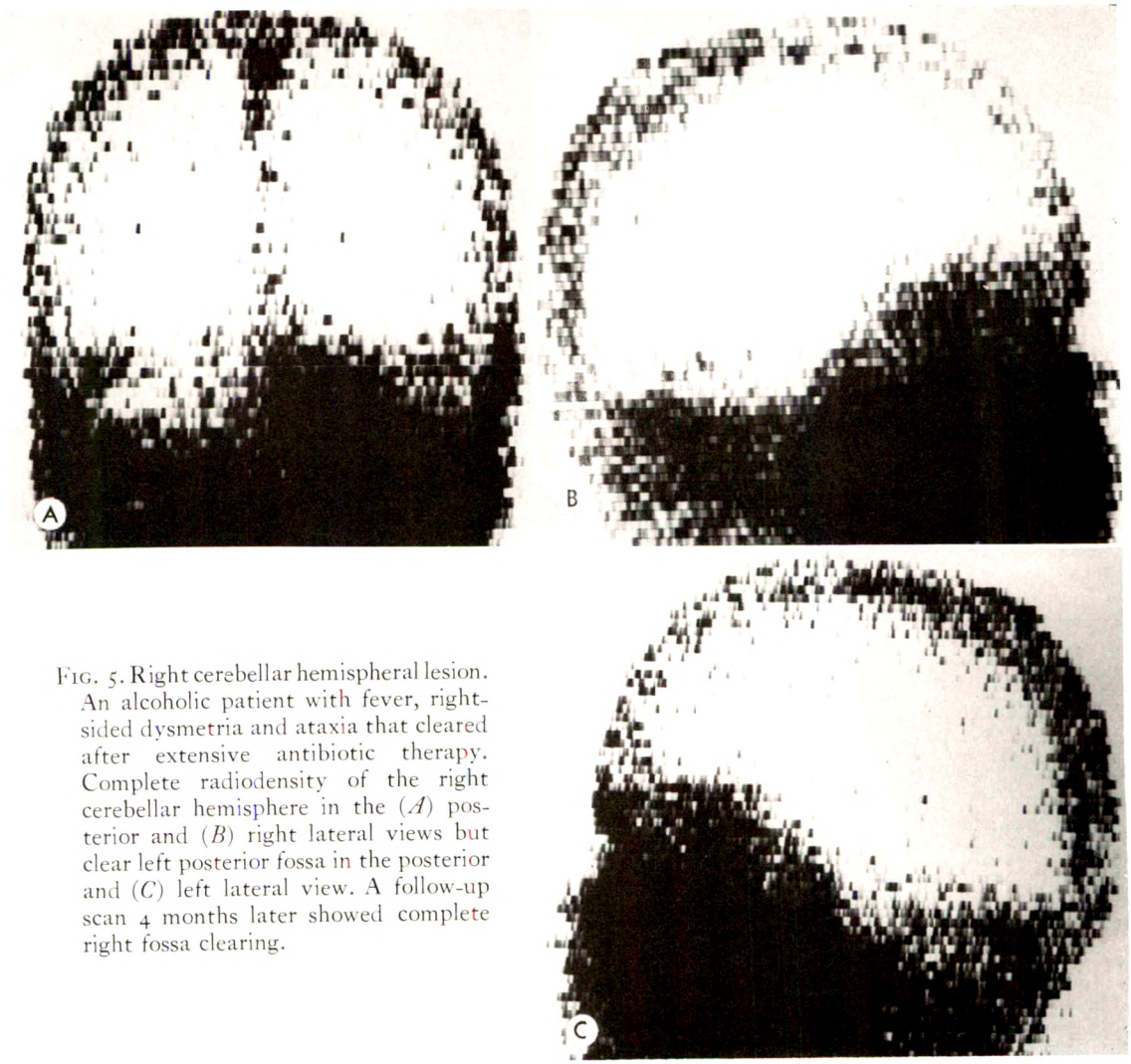


FIG. 5. Right cerebellar hemispheral lesion. An alcoholic patient with fever, right-sided dysmetria and ataxia that cleared after extensive antibiotic therapy. Complete radiodensity of the right cerebellar hemisphere in the (*A*) posterior and (*B*) right lateral views but clear left posterior fossa in the posterior and (*C*) left lateral view. A follow-up scan 4 months later showed complete right fossa clearing.

hemisphere (Fig. 4, *A*, *B* and *C*). The diagnosis in each case was established by cerebral air studies.

The high detection percentage in the posterior view reflects its selective nature in this study. A number of posterior fossa lesions were diagnosed because of the improved spatial resolution resulting from the hyperflexed head position and the sharp delineation of the superficial cerebral venous sinuses.[3,6] Figure 5, *A*, *B* and *C* is an unusual example of an extensive right cerebellar hemispheral lesion.

Our results support the routine use of the vertex view in brain scanning. We also recommend it as the initial brain scanning view in all patients presenting with nonfocal neurologic disease.

SUMMARY

To establish the value of the vertex view in routine brain scanning, 139 abnormal pertechnetate brain scans, diagnosed from 638 studies in which the vertex projection was routinely taken along with the conventional views, were evaluated for the lesions on each individual scan.

We found that the vertex view detected 89.9 per cent of the lesions; the right lateral, 41.7 per cent; the left lateral, 59.7 per cent; the anterior, 69.4 per cent; and the posterior, 81.7 per cent.

A variety of abnormalities was detected with the vertex view including 2 cystic lesions appearing as negative defects and basilar brain lesions. The selective nature of the properly positioned posterior view accounted for its high detection percentage.

The routine use of the vertex view is recommended.

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MOVEMENTS OF VENTRICULAR FLUID LEVELS DUE TO CEREBROSPINAL FLUID FORMATION*

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IT IS thought that in man, cerebrospinal fluid is formed at the rate of about 0.3 ml. per minute and that most of this is secreted by the choroid plexus of the lateral, third and fourth ventricles.[7,8,10,17,31,37,39,41]

The methods for measuring the rate of cerebrospinal fluid formation experimentally include subarachnoid drainage,[2,30] drainage from the aqueduct,[12] clearance of nondiffusable substances from the subarachnoid space,[9] rate of turnover of Na^{24}, and ventriculocisternal perfusion.[3,19,20,21]

A roentgenographic method for measuring the net rate of cerebrospinal fluid formation in the temporal horn in man has been previously described.[27]

The active secretion of cerebrospinal fluid in the lateral ventricle may be demonstrated in the dog by roentgenographic techniques. Two experiments have been described with the animal in the brow-up position, and changes of ventricular fluid levels were shown after introduction of both positive and negative contrast media by ventricular puncture.[28]

In the first experiment, a lateral ventricle was filled with air above and pantopaque below the level of the ventricular needle. Serial roentgenograms showed an accumulation of fluid of water density between the air and pantopaque. This was presumably the newly formed cerebrospinal fluid. By measuring the cross-sectional area of the lateral ventricle at the site of needle puncture, the rate of formation of cerebrospinal fluid could be assessed roentgenographically and compared with that which was aspirated directly via the ventricular needle.

The second experiment (Fig. 1, *A*, *B* and *C*) involved partial filling of the lateral ventricles via bilateral ventricular punctures with lipiodol ascendant,* a nonabsorbable hypobaric oily contrast medium. This material behaved like air and "floated" anteriorly to fill the anterior horns. It was also forced down into the third ventricle at the time of insertion. Serial roentgenograms demonstrated ascent of the oil-cerebrospinal fluid interface in the lateral ventricular body and displacement of the lipiodol ascendant from the lateral ventricle. The contrast material was then forced downwards into the aqueduct and fourth ventricle. Because of the high viscosity of lipiodol ascendant, a considerable elevation of intraventricular pressure probably occurred, so this experiment could not be used for quantitation of the rate of cerebrospinal fluid formation in the lateral ventricles.

These animal experiments suggested the possibility of measuring the rate of cerebrospinal fluid formation in the lateral ventricles of man during pneumoencephalography by utilizing the air in the brow-up position to segment the ventricular system.

PRESENT STUDY

Twenty patients who were able to cooperate were studied during routine pneumoencephalography. After good filling of the lateral ventricles was obtained in the erect position, the patients were immobilized in the supine position for 1 to 2 hours. Several patients were studied for up to 6 hours. Serial lateral and anteroposterior roentgenograms and tomograms were taken at known time intervals and with fixed predetermined magnification. Two patients were immobilized in the erect position for 4 hours to show the rate of air absorption.

* Lipiodol Ascendant manufactured by E. Fougera and Co.

* From the Department of Neuroradiology, The New York Hospital–Cornell Medical Center, New York, New York.
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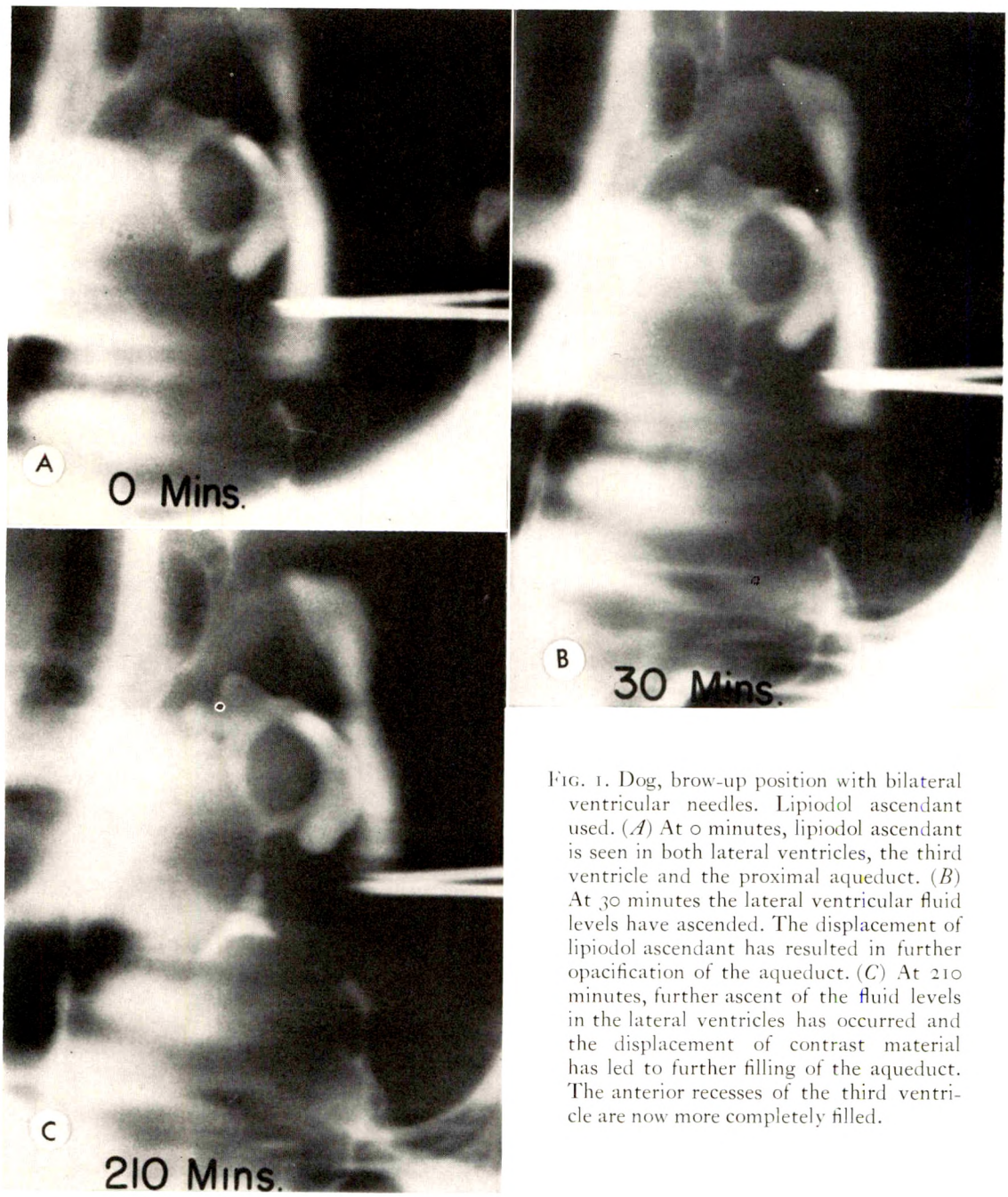


Fig. 1. Dog, brow-up position with bilateral ventricular needles. Lipiodol ascendant used. (*A*) At 0 minutes, lipiodol ascendant is seen in both lateral ventricles, the third ventricle and the proximal aqueduct. (*B*) At 30 minutes the lateral ventricular fluid levels have ascended. The displacement of lipiodol ascendant has resulted in further opacification of the aqueduct. (*C*) At 210 minutes, further ascent of the fluid levels in the lateral ventricles has occurred and the displacement of contrast material has led to further filling of the aqueduct. The anterior recesses of the third ventricle are now more completely filled.

RESULTS

LATERAL VENTRICLES

The fluid levels in the bodies of the lateral ventricles ascended towards the foramen of Monro. The rate of ascent varied from 0.26 cm. per hour to 2.8 cm. per hour, and appeared in general to be inversely proportional to the area of cross-section of the body of the lateral ventricle. In those patients with asymmetric lateral ventricles, the fluid level in the smaller ventricle ascended faster (Fig. 2, *A*, *B* and *C*).

Once the fluid levels reached the foramen

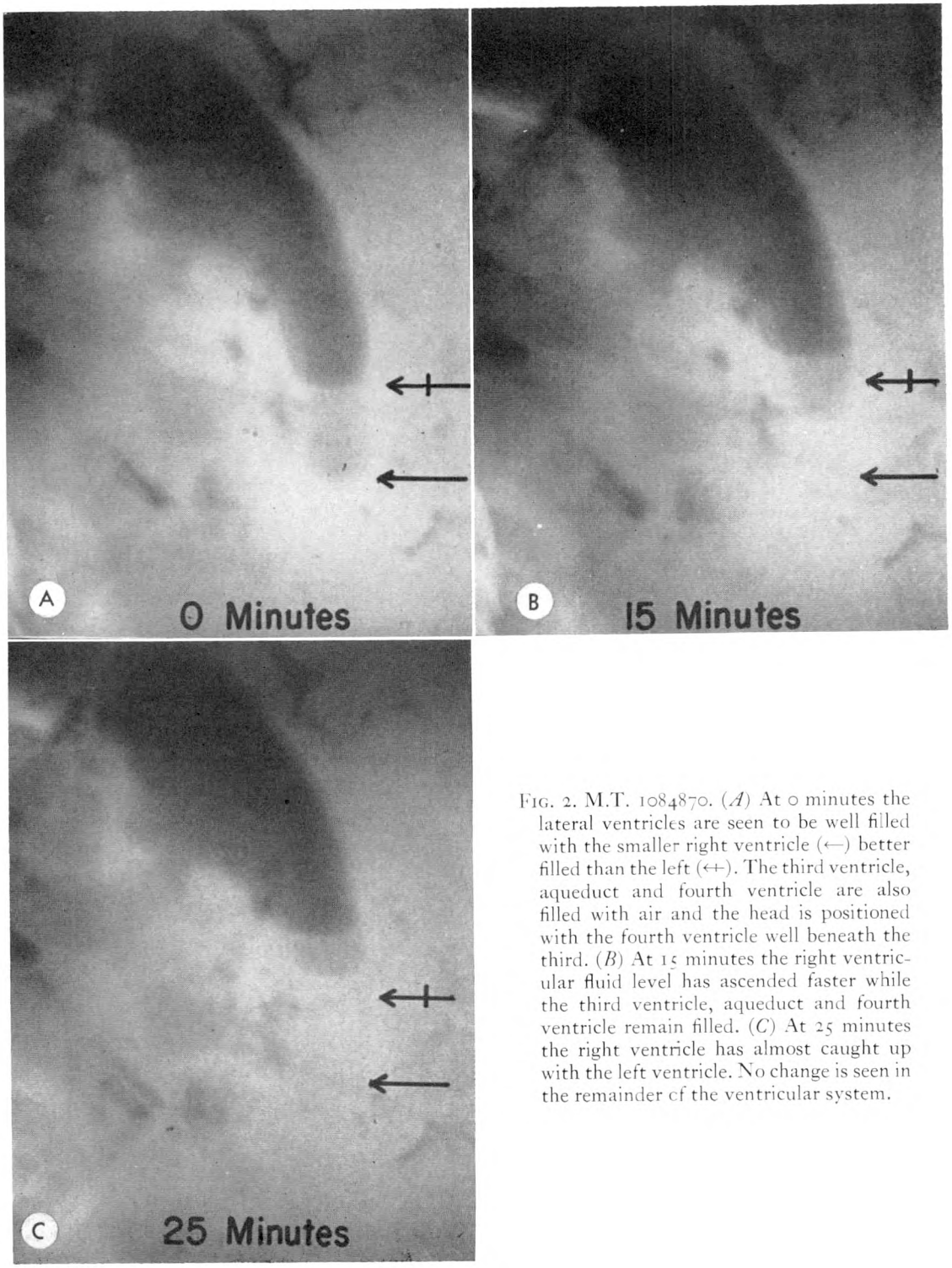


FIG. 2. M.T. 1084870. (*A*) At 0 minutes the lateral ventricles are seen to be well filled with the smaller right ventricle (←) better filled than the left (↞). The third ventricle, aqueduct and fourth ventricle are also filled with air and the head is positioned with the fourth ventricle well beneath the third. (*B*) At 15 minutes the right ventricular fluid level has ascended faster while the third ventricle, aqueduct and fourth ventricle remain filled. (*C*) At 25 minutes the right ventricle has almost caught up with the left ventricle. No change is seen in the remainder of the ventricular system.

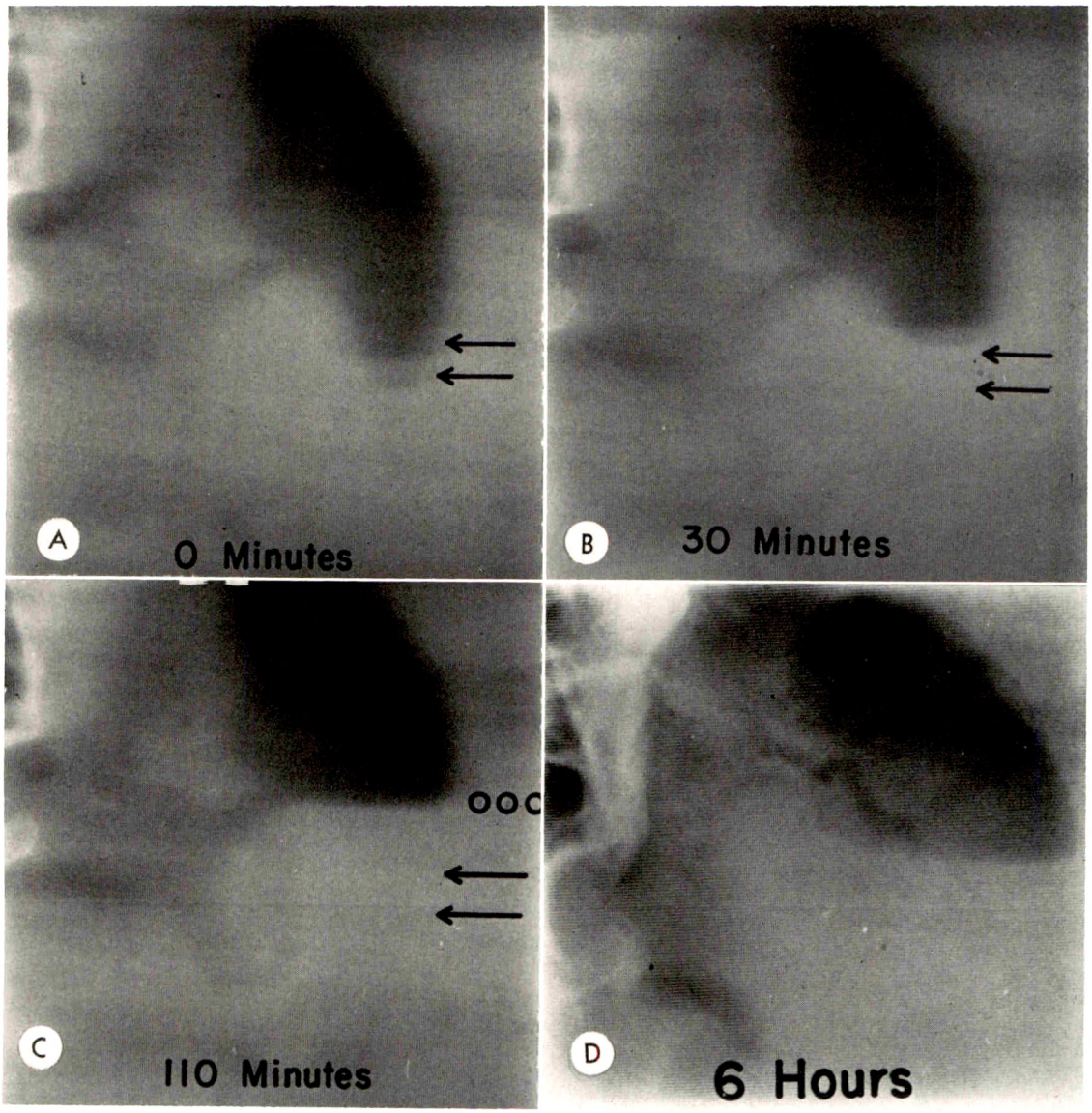


Fig. 3. R.D. 1130210. (*A*) At 0 minutes the lateral ventricular fluid levels (←) are asymmetric and the third ventricle is opacified. (*B*) At 30 minutes the lateral ventricular fluid levels have ascended. (*C*) At 110 minutes both lateral ventricles are now filled to the level of the foramen of Monro (ooo) and the third ventricle remains air-filled. (*D*) At 6 hours only a small bubble of air remains in the third ventricle.

of Monro, no further ascent occurred until the third ventricle filled with fluid (Fig. 3, *A–D*).

Several patients showed minor changes in ventricular size during the observation. The largest change was an increase of 2 mm. in the span of the frontal horns in 1 patient. Most of the cases, however, showed no measurable change during the study and no change could be detected in the lateral projections.

THIRD VENTRICLE

In most cases the third ventricle remained filled with air for the duration of the study (Fig. 2, *A*, *B* and *C*).

When a patient was immobilized for about 6 hours, the third ventricle remained

filled with air until the lateral ventricular fluid reached the foramen of Monro. After this time, as cerebrospinal fluid spilled down the third ventricle and aqueduct, there was, during the subsequent 4 hours, a slow ascent of a fluid level in the third ventricle. This fluid level continued to ascend until it reached the foramen of Monro (Fig. 3, *A–D*).

In a patient with a large suprapineal recess it was possible to observe an ascending fluid level in this dependent part of the third ventricle (Fig. 4, *A–D*). This presumably resulted from accumulation of

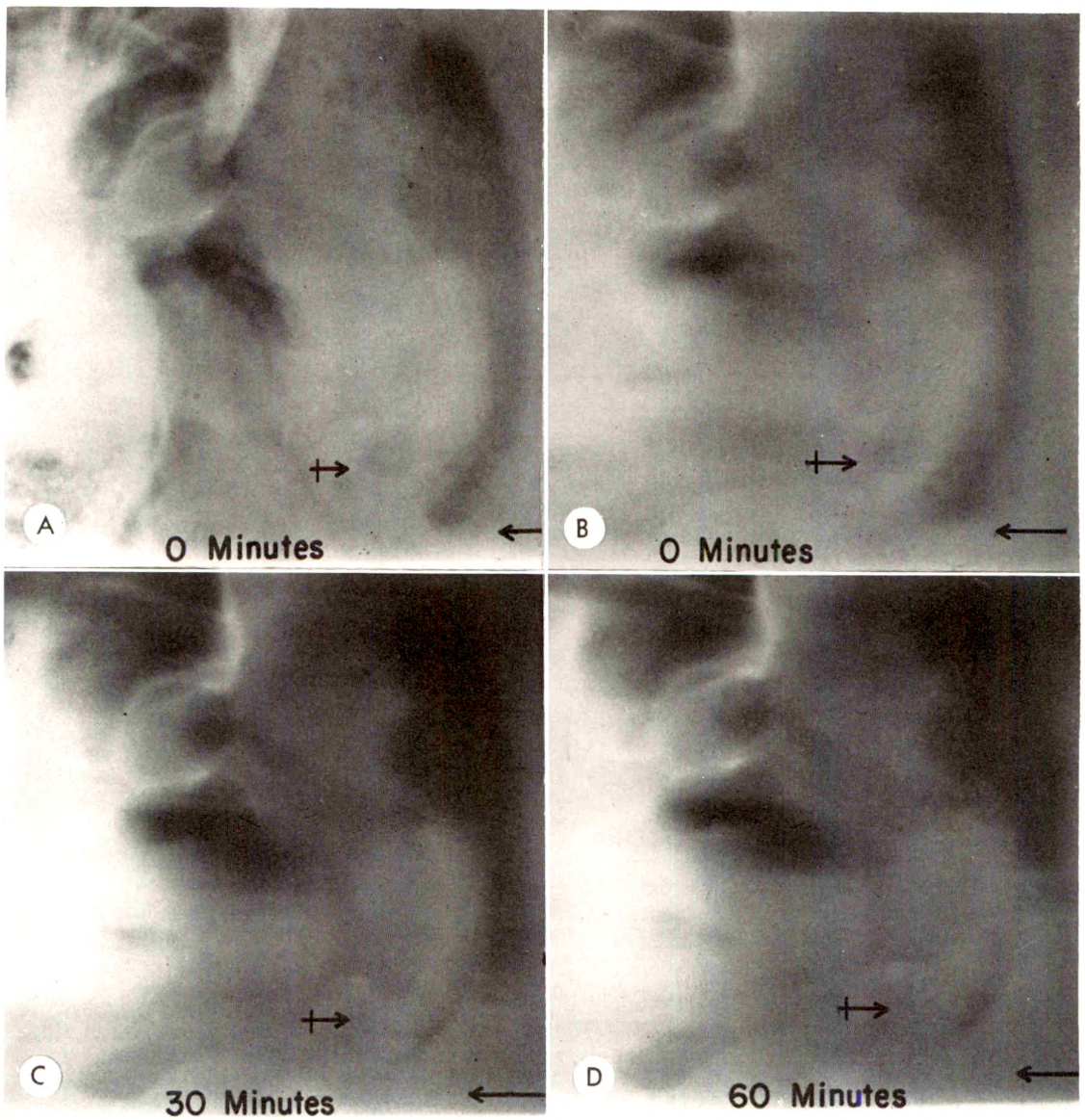


FIG. 4. B.S. 942539. (*A*) At 0 minutes the small lateral ventricles are equally well filled (←). The third ventricle is also completely filled with air and a large suprapineal recess (↔) is opacified. (*B*) Tomogram at 0 minutes also demonstrates the opacified aqueduct and fourth ventricle. (*C*) At 30 minutes, a considerable ascent of the lateral ventricular fluid levels has occurred. The suprapineal recess has partially filled with fluid. (*D*) At 60 minutes, the lateral ventricular fluid levels have ascended further anteriorly. The suprapineal recess is now completely filled with fluid but the aqueduct and fourth ventricle remain opacified.

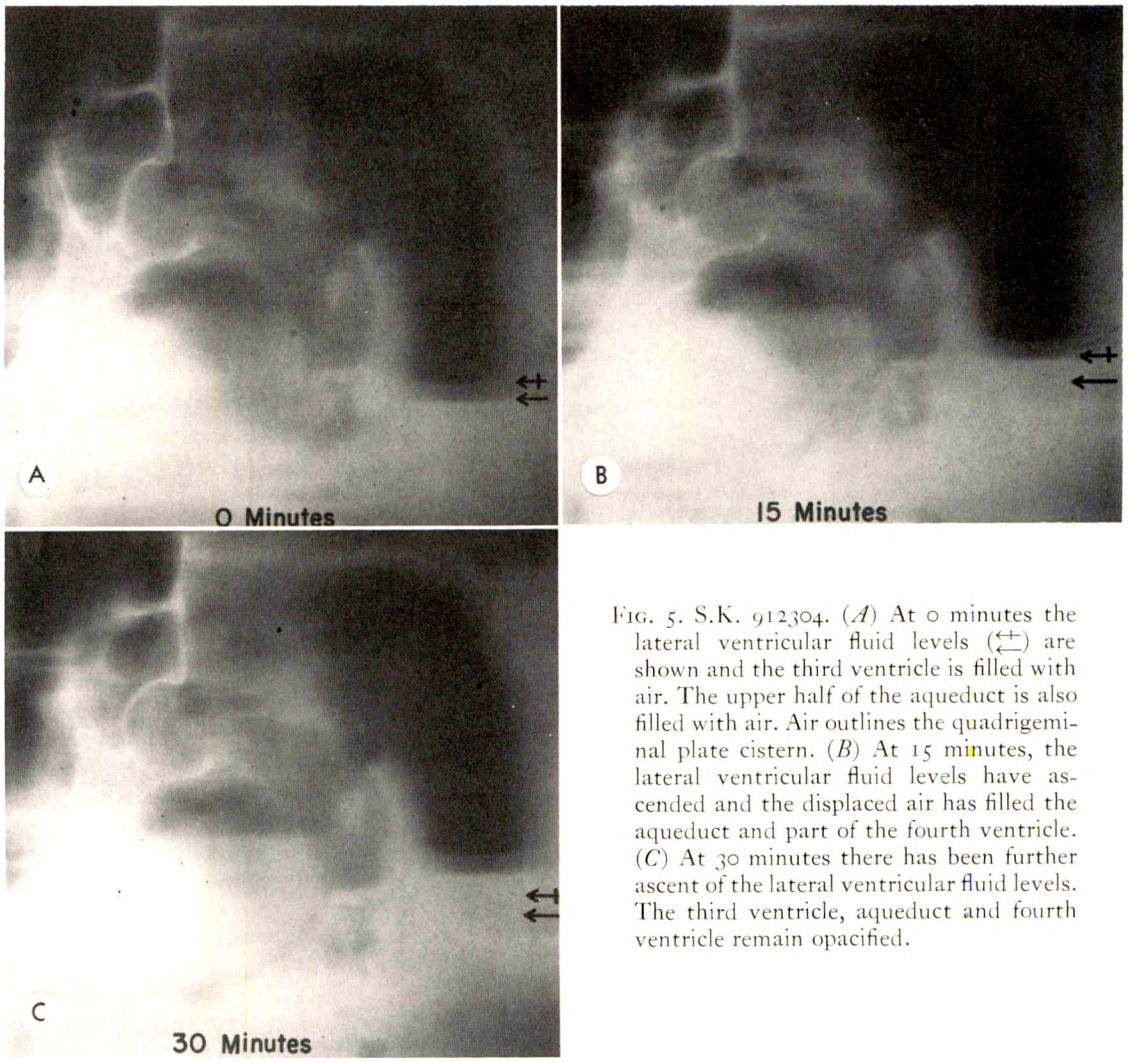


Fig. 5. S.K. 912304. (*A*) At 0 minutes the lateral ventricular fluid levels (⇄) are shown and the third ventricle is filled with air. The upper half of the aqueduct is also filled with air. Air outlines the quadrigeminal plate cistern. (*B*) At 15 minutes, the lateral ventricular fluid levels have ascended and the displaced air has filled the aqueduct and part of the fourth ventricle. (*C*) At 30 minutes there has been further ascent of the lateral ventricular fluid levels. The third ventricle, aqueduct and fourth ventricle remain opacified.

cerebrospinal fluid from the third ventricular choroid plexus.

AQUEDUCT

In many of the studies the aqueduct remained filled with air throughout (Fig. 2, *A*, *B* and *C*). In those cases where on the initial roentgenograms the third ventricle was air-filled but the aqueduct was not, a progressive filling of the aqueduct with air was observed (Fig. 5, *A*, *B* and *C*).

Once the lateral ventricular fluid levels reached the foramen of Monro, the aqueduct rapidly became filled with cerebrospinal fluid (Fig. 6, *A*, *B* and *C*). The position of the head was important in relation to aqueduct filling. Only if the fourth ventricle lay below the level of the aqueduct would air be trapped at this level. If the fourth ventricle lay above the level of the aqueduct, escape of air would be expected.

FOURTH VENTRICLE

The fourth ventricle remained air-filled in many of the cases. The position of the head was probably of importance, as prolonged opacification of this structure would only be expected when the outlets (foramina of Luschka and Magendie) lay below the level of the superior part of the fourth ventricle.

In 1 case a progressive accumulation of

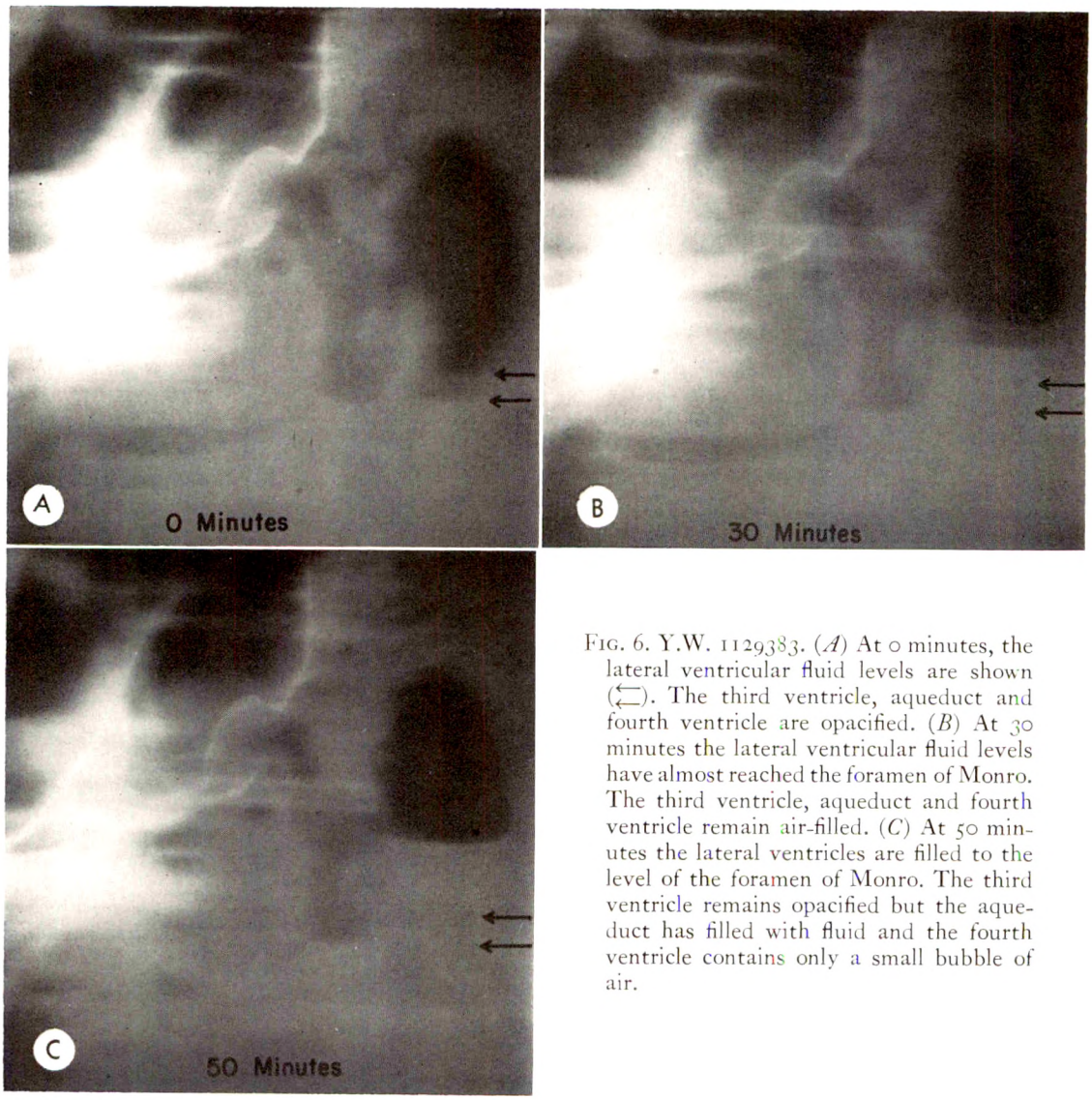


FIG. 6. Y.W. 1129383. (*A*) At 0 minutes, the lateral ventricular fluid levels are shown (⇐). The third ventricle, aqueduct and fourth ventricle are opacified. (*B*) At 30 minutes the lateral ventricular fluid levels have almost reached the foramen of Monro. The third ventricle, aqueduct and fourth ventricle remain air-filled. (*C*) At 50 minutes the lateral ventricles are filled to the level of the foramen of Monro. The third ventricle remains opacified but the aqueduct has filled with fluid and the fourth ventricle contains only a small bubble of air.

fluid in the fastigium of the fourth ventricle was demonstrated with serial midline tomograms (Fig. 7, *A*, *B* and *C*).

Once the lateral ventricles were filled to the foramen of Monro, the fourth ventricle, like the aqueduct, rapidly became fluid-filled (Fig. 6, *A*, *B* and *C*).

PROLONGED OBSERVATIONS IN THE ERECT POSITION

In order to assess the role of air absorption in the phenomena observed, 2 patients were kept sitting for 4 hours with the head immobilized. In this position, it is not possible for air to escape down the aqueduct from the lateral ventricles. The volume of air in the lateral ventricles showed no significant change during the period of observation (Fig. 8, *A* and *B*).

In both the experimental animal and in man, provided the head was immobilized in the brow-up position, predictable changes in the fluid levels of the lateral ventricles occurred. Prolonged opacification of the third ventricle, aqueduct and fourth ventricle appeared to result from active displacement of the contrast material,

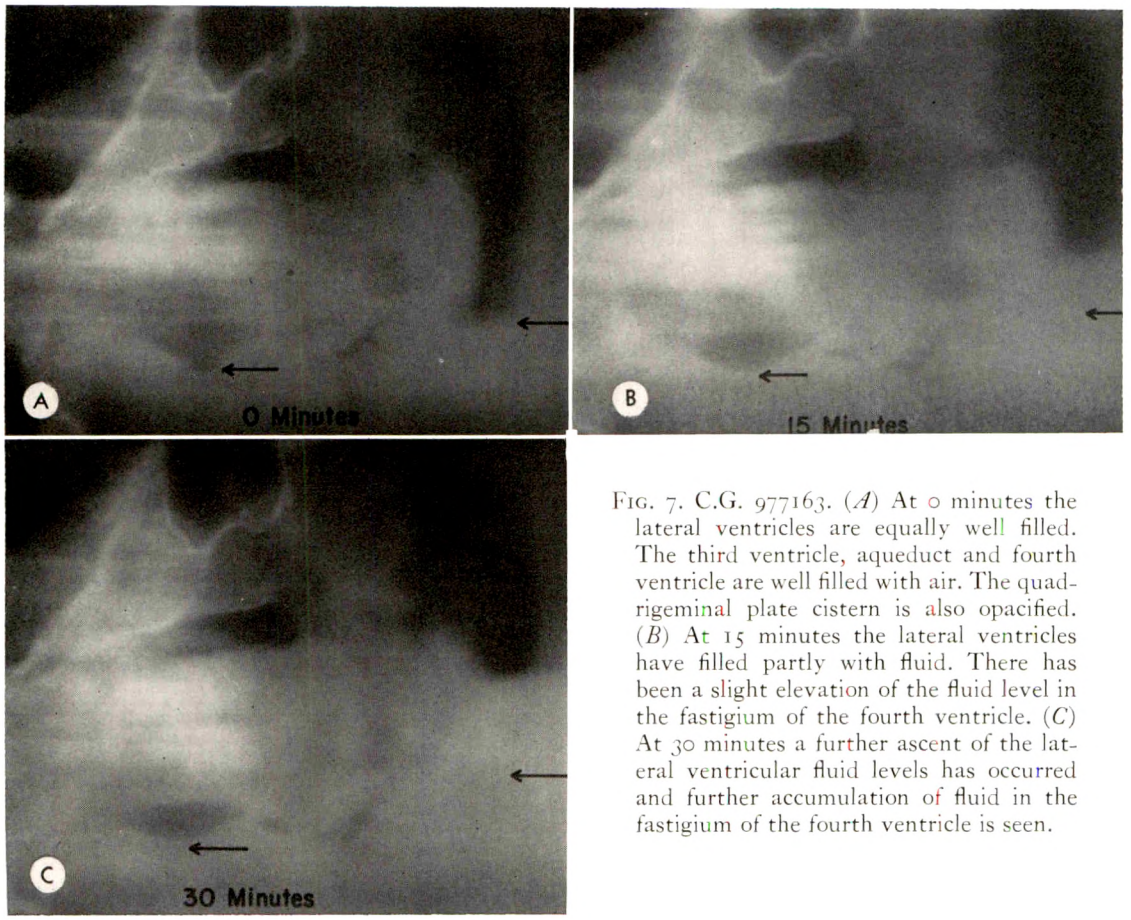


Fig. 7. C.G. 977163. (*A*) At 0 minutes the lateral ventricles are equally well filled. The third ventricle, aqueduct and fourth ventricle are well filled with air. The quadrigeminal plate cistern is also opacified. (*B*) At 15 minutes the lateral ventricles have filled partly with fluid. There has been a slight elevation of the fluid level in the fastigium of the fourth ventricle. (*C*) At 30 minutes a further ascent of the lateral ventricular fluid levels has occurred and further accumulation of fluid in the fastigium of the fourth ventricle is seen.

either air or lipiodol ascendant, by the newly formed lateral ventricular cerebrospinal fluid.

In Figure 9, 3 separate phases are shown, summarizing the changes that occur during prolonged positioning in the supine position.

Phase I. Newly formed cerebrospinal fluid accumulates in the bodies of the lateral ventricles and results in ascending fluid levels. The fluid levels ascend at a more or less constant rate until they reach the foramen of Monro. As the fluid levels ascend, gas is displaced into the third ventricle, aqueduct and fourth ventricle resulting in prolonged opacification of these structures, provided the fourth ventricle exit foramina are below the posterior part of the third ventricle.

Cerebrospinal fluid formed in the third ventricle may be seen accumulating in the suprapineal recess and also in the fastigium of the fourth ventricle.

Phase II. Once the lateral ventricles are filled with fluid to the level of the foramen of Monro, cerebrospinal fluid spills into the third ventricle and flows down the aqueduct. The aqueduct and fourth ventricle rapidly become fluid-filled, but the third ventricle fills very slowly with fluid. This slow decrease in volume of the residual gas is presumably the result of absorption, either through the ependyma or into the newly formed cerebrospinal fluid.

Phase III. Once the fluid level in the third ventricle reaches the posterior margin of the foramen of Monro, the combined fluid levels of the third and lateral ventricles gradually rise as the residual air is absorbed.

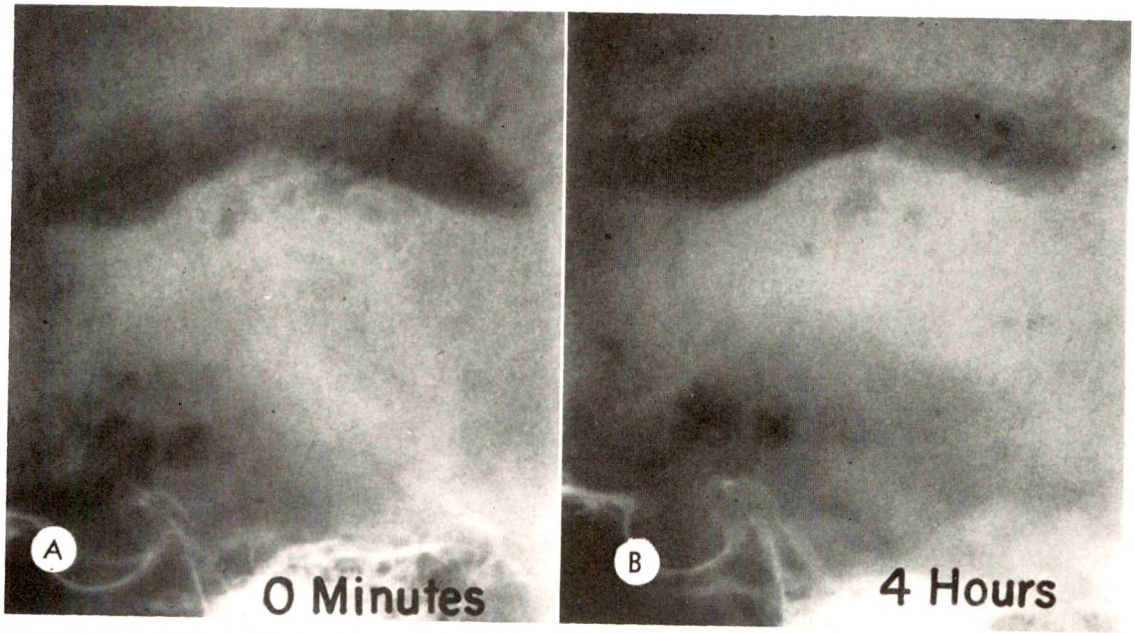


FIG. 8. V.L. 865708. (*A*) At 0 minutes with the head erect, the bodies of the lateral ventricles are shown There is some air in the interpeduncular cistern and over the cerebral hemispheres. (*B*) At 4 hours, very little change has occurred in the ventricles. There has been absorption of some of the air in the subarachnoid spaces.

The time relationships of the 3 phases varied in different individuals and depended partly upon the relative sizes of the ventricles. Phase I occurred during the first 1 or 2 hours, while Phase II lasted for about 4 hours. Phase III probably lasted for 3 to 12 days depending on the size of the lateral ventricles.

ESTIMATION OF THE RATE OF CEREBROSPINAL FLUID FORMATION IN THE LATERAL VENTRICLES

In 16 cases where the ascent of fluid levels occurred in the posterior two-thirds of the bodies of the lateral ventricles, the rate of cerebrospinal fluid formation was calculated for each lateral ventricle (Table 1).

The rates of ascent of the fluid levels were measured from superimposed tracings of 2 lateral roentgenograms taken at known time intervals.

The cross-sectional areas of the bodies of the lateral ventricles were also calculated from tracings. Coronal tomograms were used when available and the average area was used when two or more tomographic levels had been obtained.

The rate of cerebrospinal fluid formation in each lateral ventricle and also the total formed by both lateral ventricles are shown in Table 1.

There was considerable variation from subject to subject, the lowest rate of cerebrospinal fluid formation being 0.023 ml./min. and the highest 0.135 ml./min. with an average value of 0.071 ml./min.

DISCUSSION

The disappearance of gaseous contrast media from the ventricular system during and after pneumoencephalography and ventriculography may result from 3 different mechanisms.

The position of the head plays a vital role in the loss of gas from the lateral ventricles. When the fourth ventricle is placed higher than the foramen of Monro, as in the "hanging head" position, gas will bubble out rapidly. A similar loss of gas will occur sometimes when the head is turned laterally from the supine position, as during

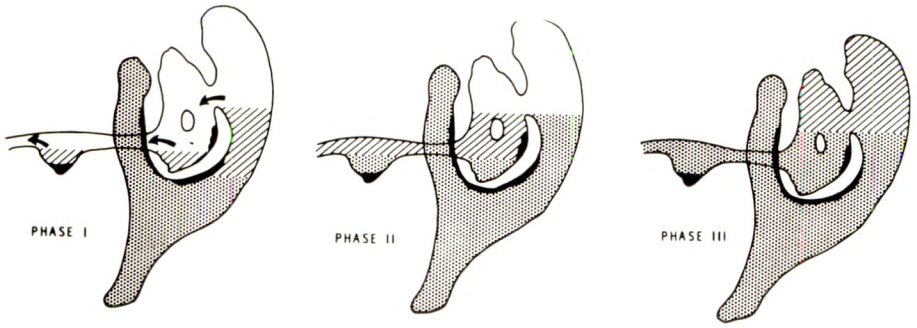


Fig. 9. The 3 phases of disappearance of air from the ventricular system in the brow-up position are shown.

maneuvers for filling the temporal horns.

Absorption of gas into the blood stream either via the cerebrospinal fluid or directly through the ependyma also occurs. This is particularly obvious when gases with a high solubility are used. Carbon dioxide, nitrous oxide and ethylene show a more rapid disappearance from the ventricles than air, but the most striking difference is seen in the subarachnoid spaces over the cerebral hemispheres and also in the cisterns.[1,18,25,29]

When xenon is employed, an initial rapid phase followed by a slow phase of disappearance has been presumed to be the result of diffusion of oxygen and nitrogen from the blood stream into the ventricles.[25] It appears, however, that, at least with air, absorption plays a minor role in the rapid initial emptying phase and that the period of absorption may extend over a week or more. A more rapid absorption of air occurs over the cerebral hemispheres and this is usually almost complete after 24 or 48 hours.

The third mechanism involved in the egress of air from the ventricles occurs when the head is placed in a brow-up position. The lateral and third ventricles then resemble an inverted U-tube connected by the foramen of Monro. The ∩ is closed on the lateral ventricular limb with the other limb open into the subarachnoid space. Increasing the volume of fluid in the blind limb must result in displacement of air into the other limb and downwards towards the opening into the subarachnoid space, provided the volume of the system does not increase.

Apart from providing a possible method of measuring the rate of cerebrospinal fluid formation in the lateral ventricles, these observations would seem to explain the occasional difficulty in obtaining good lateral ventricular filling in the supine position when the ventricles are small. Any delay between placing the patient in the brow-up position and obtaining the roentgenogram will allow accumulation of cerebrospinal fluid to displace the air from the lateral ventricles. In view of these findings, the authors have changed the routine for pneumoencephalography so that after the erect roentgenography is completed, the "brow-down" series is taken, followed by the brow-up supine views. Immediately after the actual roentgenograms are taken, the patient is placed in the erect position to prevent further escape of air while the brow-up views are processed and checked.

The ease of opacifying the aqueduct in the supine position may be helpful in those cases where there was poor visualization of this structure in the erect roentgenograms.

Changes in ventricular size during and after pneumoencephalography have been described. Stewart[38] observed an average increase on 24 hour roentgenograms but this was not statistically significant. Jirout,[14] Petrov,[24] and Schatzki *et al.*[34] attributed these changes to brain edema. Paul and Erickson[22] showed a reduction in

TABLE I

PATIENTS EXAMINED AND ESTIMATION OF RATES OF CEREBROSPINAL FLUID FORMATION

Name and Identification Number	Age	Diagnosis	Rate of Ascent of Lateral Ventricular Fluid Levels (cm./hr.)	Cross-sectional Area of Lateral Ventricle ($cm.^2$)	Rate of Cerebrospinal Fluid Formation in Lateral Ventricles (ml./min.)	
					Individual Ventricles	Total Lateral Ventricular Cerebrospinal Fluid
D.R. 475411	60	Unilateral Parkinson's disease	R. 0.66 L. 0.66	R. 1.25 L. 0.82	R. 0.014 L. 0.009	0.023
M.C. 1135941	34	Pseudotumor cerebri	R. 2.14 L. 1.87	R. 0.38 L. 0.36	R. 0.0135 L. 0.0112	0.025
P.S. 1138406	53	Pseudotumor cerebri	R. 1.4 L. 1.85	R. 0.69 L. 0.53	R. 0.016 L. 0.016	0.032
B.S. 942539	28	Pseudotumor cerebri	R. 1.86 L. 2.4	R. 0.52 L. 0.45	R. 0.0162 L. 0.018	0.034
N.A. 112327	33	Focal seizures	R. 2.34 L. 2.34	R. 0.61 L. 0.64	R. 0.023 L. 0.024	0.047
A.H. 1128144	34	Galactorrhea, Forbes' syndrome	R. 1.6 L. 1.6	R. 0.81 L. 1.02	R. 0.0215 L. 0.027	0.048
F.B. 1092898	69	Cerebral atrophy	R. 0.6 L. 0.26	R. 3.15 L. 4.12	R. 0.031 L. 0.018	0.049
M.R. 1123950	47	Cerebral atrophy	R. 2.4 L. 2.4	R. 0.78 L. 0.88	R. 0.031 L. 0.034	0.065
C.B. 1127430	65	Cerebral atrophy	R. 0.87 L. 1.27	R. 2.68 L. 1.86	R. 0.039 L. 0.039	0.078
P.O. 1047327	62	Dementia, Parkinson's disease, Communicating hydrocephalus	R. 0.71 L. 0.71	R. 2.9 L. 3.7	R. 0.035 L. 0.044	0.079
C.G. 977163	31	Pseudotumor cerebri	R. 2.86 L. 2.86	R. 0.97 L. 1.03	R. 0.046 L. 0.049	0.095
L.M. 1131027	26	Pseudotumor cerebri	R. 1.46 L. 1.74	R. 1.89 L. 1.69	R. 0.046 L. 0.049	0.095
H.O. 925882	56	Hemianopsia, cause uncertain	R. 1.4 L. 1.4	R. 2.12 L. 2.12	R. 0.049 L. 0.049	0.098
M.G. 1130084	47	Glioma right thalamus	R. 1.33 L. 2.14	R. 2.33 L. 1.76	R. 0.052 L. 0.062	0.114
Y.W. 1129383	49	Right parasagittal meningioma	R. 2.14 L. 2.14	R. 1.69 L. 1.58	R. 0.06 L. 0.057	0.117

Table I (*Continued*)

Name and Identification Number	Age	Diagnosis	Rate of Ascent of Lateral Ventricular Fluid Levels (cm./hr.)	Cross-sectional Area of Lateral Ventricle ($cm.^2$)	Rate of Cerebrospinal Fluid Formation in Lateral Ventricles (ml./min.)	
					Individual Ventricles	Total Lateral Ventricular Cerebrospinal Fluid
S.K. 912304	45	Cerebral atrophy	R. 1.46 L. 1.46	R. 2.82 L. 2.72	R. 0.069 L. 0.066	0.135
M.T. 1084870	31	Multiple sclerosis	R. 3.7 L. 2.10	—	—	—
R.D. 1130210	37	Ataxia—etiology not known	—	—	—	—
V.L. 865708	34	Temporal lobe epilepsy	—	—	—	—
R.I. 1084681	25	Pituitary adenoma	—	—	—	—

the ventricular size on 24 hour roentgenograms taken in the erect position.

Enlargement of the anterior horns and anterior parts of the ventricular bodies was demonstrated on 24 hour studies by Schatzki *et al.*[34] and by LeMay,[15] who also showed some change at 3 hours. All these reports were concerned with routine studies and there was no control of the head position between the initial and delayed roentgenograms. Large quantities of air were also used with extensive filling of the subarachnoid spaces.

Cobble and Brackett[5] had a unique opportunity to study ventricular size over a 3–6 hour period in patients undergoing stereotactic procedures. The heads were immobilized in the stereotactic device for the period of observation and changes in ventricular size and shape were observed. Forty of these patients had air introduced via lumbar puncture with 20–150 ml. apparently used (average 80 ml.). It was not clear whether the changes in ventricular size were similar in the 2 groups; 1 had air introduced into the lumbar region and the other had small quantities injected directly into the ventricles. It may be that some of these changes resulted directly from the stereotactic surgical procedure, as this was apparently performed in the interval between the 2 roentgenograms on which measurements were performed.

Striking changes in ventricular size may be seen in the dog when the intraventricular pressure is altered, and Cronquist *et al.*[6] have shown changes in intraventricular pressure in humans undergoing pneumoencephalography and ventriculography. Only minor pressure changes were seen, however, in patients without obstruction to the ventricular system and no persistent elevation of pressure occurred after assuming the recumbent position. It is likely that large quantities of air over the cerebral hemispheres affect the relative pressures in the intra- and extraventricular subarachnoid space.

If the aqueduct and fourth ventricle remain filled with air as the lateral ventricular cerebrospinal fluid accumulates, and if only small quantities of subarachnoid air

are present over the cerebral hemispheres, very little change of the ventricular pressure would be anticipated. Therefore there would be no appreciable change in ventricular size.

The rates of cerebrospinal fluid formation in the lateral ventricles in 16 patients were calculated by a simple volumetric method. The average value for both lateral ventricles combined was 0.07 ml./min., and a considerable individual variation was present (Table 1). The total cerebrospinal fluid formation (bulk flow) is thought to be about 0.3 ml./min. and the discrepancy between the calculated and expected rates of cerebrospinal fluid formation is difficult to explain. Bering and Sato[3] have suggested that in the dog only one-third of the total cerebrospinal fluid formation occurs in the lateral and third ventricles, while the remaining two-thirds are formed in the fourth ventricle and extraventricularly. The evidence for this cannot be accepted without reservation, however, according to Davson.[8]

The rate of cerebrospinal fluid formation in the individual ventricles in man is not known. If the rate of total cerebrospinal fluid formation in different mammalian species is related to the mass of choroid plexus, a fairly constant figure is obtained; *i.e.*, 0.17–0.23 ml./min./gm. choroid plexus in man; 0.26–0.35 in the dog; 0.36 in the goat; and 0.37 in the cat. In man the cerebrospinal fluid may be formed in the individual ventricles in amounts proportional to the mass of choroid plexus in the ventricle.

According to Voetmann,[40] the mass of choroid plexus in 1 lateral ventricle is 0.350–1.990 gm. (mean 0.861 gm.) so 1 lateral ventricle should form 0.06–0.45 ml./min. with an average of 0.14–0.19 ml./min.

The cerebrospinal fluid formation in this series of cases was still lower than the estimated figure so that other mechanisms may be exerting their influence.

Schatzki *et al.*[34] suggested that the slight ventricular dilatation which they observed on 24 hour roentgenograms may have been due to hypersecretion of cerebrospinal fluid. Assessment of the effects of air on cerebrospinal fluid formation is being carried out at present on dogs, using ventriculocisternal perfusion before and after insertion of 1–3 cc. air. Preliminary results indicate that air in the subarachnoid space and ventricles does not alter the rate of cerebrospinal fluid formation. There has been no evidence to suggest a decrease in cerebrospinal fluid formation due to the presence of air.

Despite the apparent constancy of ventricular size, as measured by the anterior horns, it is conceivable that enlargement occurred in the nonvisualized parts of the ventricular system, particularly in the temporal horns adjacent to the choroid fissure.

The dehydration and sedation prior to pneumoencephalography and the systemic changes occurring after introduction of air may all result in a decrease in the rate of cerebrospinal fluid formation.

CONCLUSION

Observations were made on humans and animals during contrast studies of the ventricular system with the head in the brow-up position. Contrary to popular belief, air absorption appeared to play a minor role in the changes that were seen. The active secretion of cerebrospinal fluid in the lateral ventricles resulted in displacement of air from the lateral ventricles into the third ventricle, aqueduct and fourth ventricle.

In view of the rapid expulsion of air in individuals with small lateral ventricles, it would be reasonable to modify the existing pneumoencephalographic technique so that the patient lies supine in the brow-up position for the shortest time possible, and assumes the erect position while roentgenographic processing is being performed. It would also seem reasonable to perform brow-down studies first, as there is no escape of ventricular air in this position. The prolonged opacification of the aqueduct in the supine position may be useful if this structure was poorly defined on the erect roentgenograms.

A method for determining the rate of

cerebrospinal fluid formation in the lateral ventricles of man is presented. Although the contribution of the individual ventricles to the total cerebrospinal fluid formed is not known in man, the values for the lateral ventricles are lower than expected and possible factors, such as change in cerebrospinal fluid formation due to the presence of air, undetected changes in ventricular size, and systemic factors have been discussed. Elucidation of the role of many of these factors may result from experimental work in animals.

SUMMARY

Experiments in dogs and observations on human subjects during pneumoencephalography have shown that with the head in the brow-up position, ascending fluid levels in the lateral ventricles are due to active formation of cerebrospinal fluid. This accumulation of cerebrospinal fluid displaces air down the aqueduct and fourth ventricle, which may remain opacified for several hours.

Using roentgenographic measurements of the rate of ascent of lateral ventricular fluid levels and a cross-sectional area of the posterior two-thirds of the lateral ventricular bodies, the rate of cerebrospinal fluid formation in the lateral ventricles was calculated in 16 patients. The average cerebrospinal fluid formation for the lateral ventricles was about one-quarter of the accepted total cerebrospinal fluid formation (bulk flow). Possible reasons for this low figure are discussed.

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A CINEMYELOGRAPHIC STUDY OF CEREBROSPINAL FLUID DYNAMICS*

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THE slow flow of oil-soluble contrast medium in the spinal canal is familiar to every myelographer. Pulsatile motion of contrast medium may also be seen at fluoroscopy. In this communication, however, we wish to call attention to a rapid and extensive movement of contrast material that takes place on jugular compression. These observations are of interest both for the demonstration of the physiologic events underlying the Queckenstedt test, and as a possible additional diagnostic aid in myelography.

Decker[1] briefly stated that with fluoroscopy, cervically located contrast media could be seen to move caudad "slowly" on jugular compression. He gave no specific time data or further comments. The obvious explanation for this cerebrospinal fluid flow is that it is secondary to an increase in cerebrospinal fluid pressure from intracranial venous congestion. Queckenstedt[8] originally suggested that dilatation of the upper spinal venous plexuses also contributes to the induction of this cerebrospinal fluid flow, and, more recently, Taylor[9] has emphasized this point. On the basis of extensive combined cisternolumbar and lumbar isometric recordings of the Queckenstedt response, Gilland[2] concluded that in normal patients the dynamic fluid events take place within a few tenths of a second. He also estimated[3] that the cerebrospinal fluid flow past the midthoracic level on bilateral jugular compression was on the order of several (2–7) milliliters. These data would imply that bilateral jugular compression should bring about a several centimeter caudal movement of cerebrospinal fluid within a few tenths of a second. To the best of our knowledge, no quantitative studies of these dynamic events have previously been made.

MATERIAL AND METHODS

Eight patients were studied, 4 of whom had no spinal obstructive process. The clinical data are summarized in Table 1, including the myelographic findings in each case.

The roentgenographic equipment used was a General Electric Fluorocon unit with a 35 mm. cine attachment.

Pantopaque was introduced into the lumbar subarachnoid space at approximately the 3rd lumbar level with the patient prone; 15–18 cc. contrast medium was slowly injected under fluoroscopic control. Queckenstedt tests were performed with the contrast material column in the cervical, thoracic and lumbar regions with the patient in a horizontal prone position.

Bilateral jugular compressions[8] were executed with prompt initiation and firm pressure, particularly over the sides of the neck, as described elsewhere.[4] The patients were told to breathe normally and not to strain. As a rule the compressions lasted 5 seconds. The lumbar pressure changes during the Queckenstedt maneuver were measured isometrically with a small, lightweight (4 gm.) Statham No. SP 37 pressure transducer connected to a single-stage amplifier and a Midwestern 621 HT light

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TABLE I

SUMMARY OF CLINICAL, MANOMETRIC, AND MYELOGRAPHIC DATA IN 8 PATIENTS SUBJECTED TO CINEMYELOGRAPHY

Case	Name Age Sex	Clinical Data	Electro-manometrics	Myelogram	Diagnosis
1	V.S. 53 M	Sudden paraplegia 8 months ago with partial recovery. Then progressive pain and leg weakness past 1 month	Normal	Normal	Transverse myelitis
2	E.M. 54 M	4 years of low back pain. Bilateral L_4 decompression 2 years ago. Large L_5–S_1 disk protrusion removed after cine study	Normal	Defects L_4–5 and L_5–S_1?	Multiple lumbar disk herniations
3	R.A. 28 M	2 years low back pain and right leg sciatica. Neurologic deficit L_5–S_1	Normal	L_4–5 left? root sleeve defect	L_4–5 disk herniation
4	A.G. 73 M	1 year of progressive leg weakness and pain. Spastic paralysis, moderate parahypoesthesia and arm atrophy and weakness	Normal	Essentially normal. No cervical cord atrophy, but slight splaying	Myelopathy of unknown etiology. Atypical ALS ? Spondylotic myelopathy ? ?
5	J.D. 50 M	2 months right body pain initially up to ear, later only D8–L2 area. No neurologic deficit	Normal	Normal	Psychogenic or organic (cerebral) transient hemi-pain
6	P.G. 56 F	1 year post-traumatic right arm pain and hypoesthesia. Decreased pin-prick right arm	Normal	Normal	Post-traumatic cervical rhizopathy
7	M.R. 52 F	4 months right arm numbness and parenthesia. Neurologic: right arm hypalgesia of functional character. No objective deficit	Complete block with head in full extension, marked block with head neutral, small block in full extension	Minor disk protrusion C5–6 right side	Minor cervical disk protrusion with rhizopathy and functional aggravation
8	B.B. 39 M	1 year right leg weakness, subsequently also both arms. Hyperactive deep tendon reflexes legs, hand muscle atrophy	Complete block in full extension, marked block in other positions	Persistent defect at C5–6	C5–6 disk protrusion with cord compression (verified on surgery)

beam recorder.[6] Normally, the pressure rise to the higher "plateau" level occurs in less than 0.5 seconds on jugular compression, to fall again equally fast on release of the compression. This sequence appears as a "square wave" response on the recordings (Fig. 1*A*).

The contrast medium dynamics were observed on the fluoro-TV screen and simultaneously recorded on movie film at 30 frames per second. Compression initiation was recorded with a lever connected to the examiner's hands, when these were not included in the field of view directly. For analysis, print enlargements were made from appropriate film strips to allow precise measurement of the extent and timing of contrast material movement (Fig. 1, *B–D*). Magnification errors were corrected and the distances reported in Table II are computed anatomic measurements.

The following values were calculated from the recorded data: the time between onset of compression and peak (maximum) contrast velocity (V_{max}); and the average contrast velocity (V_{ave})—the total distance traveled by the contrast material column divided by the time required to traverse that distance. The distention of the lumbar sac on jugular compression was expressed as per cent increase in lateral diameter (averaged from several levels) and also as

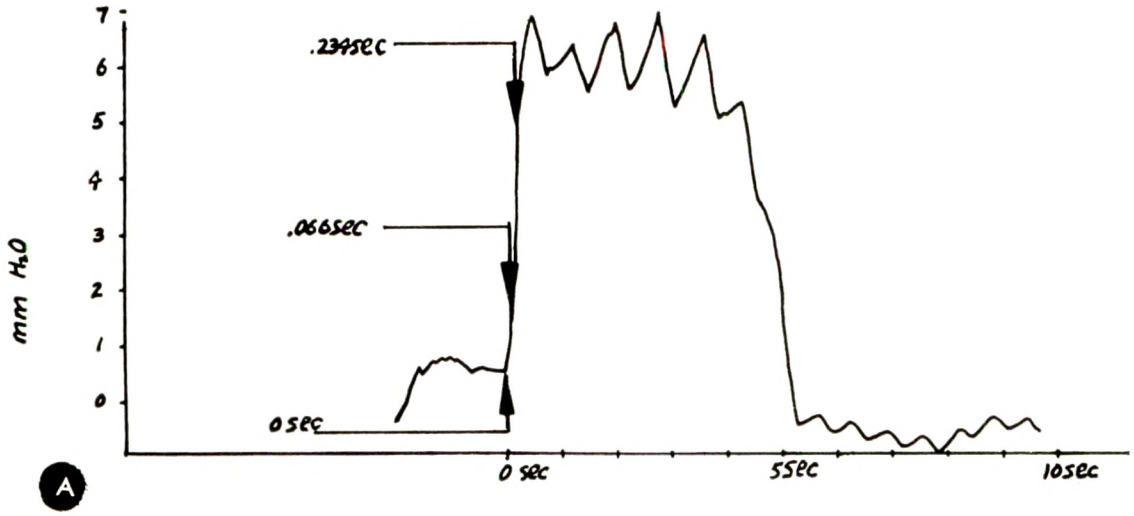


Fig. 1. Case 6. (*A*) Normal electromanometric Queckenstedt response. Note the essentially "square wave" appearance with the rapid pressure rise and fall phases occurring within 0.5 seconds.

the estimated percentage of volume increase, assuming a cylindrical model. The data are summarized in Table 11.

RESULTS

CERVICAL CANAL

The time from the onset of compression to the visualization of contrast medium movement was almost immediate (Fig. 1, *B-D*). The average time between the onset of compression and the V_{max} was 1/15 of a second. The V_{max} varied between 11 and 43 cm. per second, and the V_{ave} between 5 and 15 cm. per second. The maximum distance of contrast material travel varied between 3 cm. to more than 10 cm.

THORACIC CANAL

The contrast medium movement in the thoracic canal was almost as rapid as in the cervical canal. The V_{max} in the 2 patients with unobstructed cerebrospinal fluid flow was 9 and 23 cm. per second, respectively, and the V_{ave} 8 and 13 cm., respectively. The V_{max} occurred approximately 1/15 of a second after the onset of compression.

LUMBAR CANAL

In the lumbar region it was noted that the contrast medium column did not move downward very rapidly, although there was a slow downward shift over the first 2–4 seconds of compression in the upper lumbar canal. In the lower lumbar canal the main movement noted was a lateral distention (Fig. 2, *A* and *B*). This distention amounted to an increase in lateral diameter ranging from 28 to 50 per cent. The computed volume increase averaged 84 per cent.

An interesting finding in the lumbar region was that with the Queckenstedt maneuver, one could force contrast medium out into the root sheaths (Fig. 3, *A* and *B*). This particular maneuver may be of significant value in bringing out defects from lumbar disk protrusions.

In summary, prompt bilateral jugular compression brought about a very rapid downward movement of contrast material in the cervical and thoracic regions, appearing almost instantaneous on direct observation. The movement was always completed within 0.5 seconds in the subjects without spinal obstructive processes. The distance of contrast medium movement was about 3 to 5 vertebral bodies. In the lower lumbar canal there was no appreciable downward shift, but instead an average 38 per cent increase in diameter of the sac and improved visualization of the root sleeves.

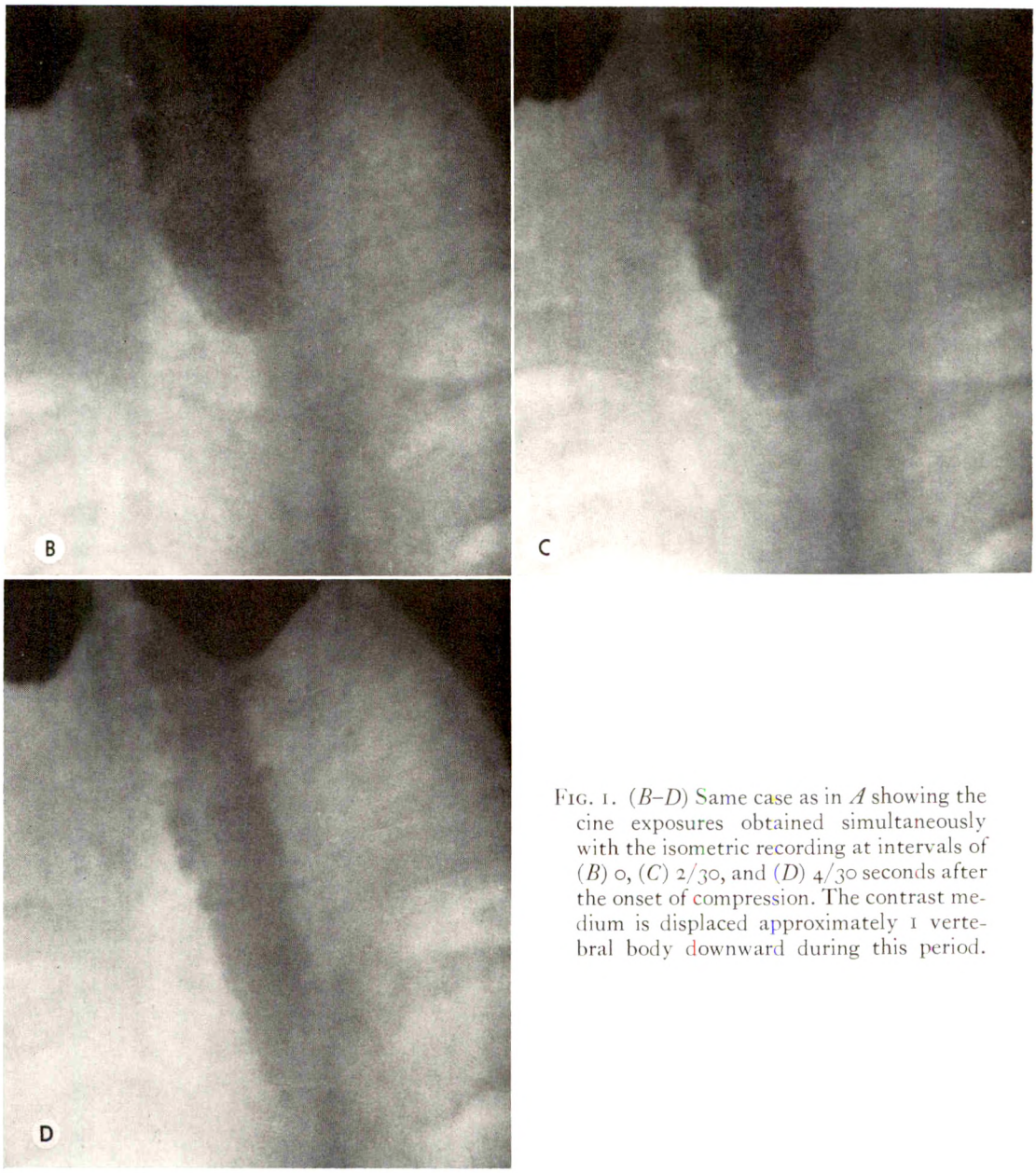


FIG. 1. (*B–D*) Same case as in *A* showing the cine exposures obtained simultaneously with the isometric recording at intervals of (*B*) 0, (*C*) 2/30, and (*D*) 4/30 seconds after the onset of compression. The contrast medium is displaced approximately 1 vertebral body downward during this period.

DISCUSSION

The findings confirm the assumption that a rapid and substantial cerebrospinal fluid flow is induced by prompt jugular compression, as inferred from isometric recordings. It is obviously futile to try to study these events accurately with the slow lumbar open-end manometer, as is common clinical practice. A rather marked spinal obstruction will be needed to cause the open-end manometric response to deviate from the normal. With high fidelity isometric transducer recording, even slight impairment of cerebrospinal fluid flow due to an obstruction will readily be detected by a prolonged pressure rise time.[5]

It is of interest to note that Poppen and Hurxthal[7] proposed that in order for a spinal obstruction to be detectable with open-end manometrics, the cross-sectional

TABLE II

RESULTS OF CINEMYELOGRAPHIC MEASUREMENTS

Case Sex Age	Maximum Cervical Velocity (V_{max})	Maximum Thoracic Velocity (V_{max})	Average Velocity (V_{ave})	Total Time of Movement	Extent of Movement	Lumbar Sac Distention in mm., per cent Diameter Increase, and Estimated Volume Increase
1. V.S. M 53	43 cm./sec.		11.1 cm./sec.	0.3 sec.	3.7 cm. +	+ 5.3 mm. 50 per cent diameter increase 122 per cent volume increase
2. E.M. M 54	30 cm./sec.				10 cm. +	
3. R.A. M 28	10.8 cm./sec.		5.4 cm./sec.	1.3 sec.	7 cm.	
4. A.G. M 73	30 cm./sec.		15 cm./sec.	0.2 sec.	3 cm.	
5. J.D. M 50		9 cm./sec.	7.5 cm./sec.	0.2 sec.	1.5 cm.	
6. P.G. F 56		23 cm./sec.	12.8 cm./sec.	0.4 sec.	5.3 cm.	+ 3.3 mm. 28 per cent diameter increase 42 per cent volume increase
7. M.R. F 52		None	None			+ 7.5 mm. 35 per cent diameter increase 89 per cent volume increase
8. B.B. M 39 (Complete block)	0 cm./sec.		0 cm./sec.	0	0	0 0 0

area of the spinal canal at the obstruction must be less than the bore of the needle. They considered the Queckenstedt-induced flow past an obstruction to equal the outflow into the open-end tube, on the assumption that the spinal theca was essentially rigid. In fact, the outflow into an open-end manometer is in the order of 0.5 to 1.5 ml. only, (depending on the manometer bore and Queckenstedt response amplitude), as compared to the several additional milliliters of cerebrospinal fluid being accommodated inside the expanding lumbar sac. If Poppen and Hurxthal's theory had been correct, it would be impossible to detect spinal obstruction with isometric transducers as long as any communication existed between the cerebrospinal fluid above and below the block. Pressure changes in a rigid system would be transmitted to all points perfectly well until the block was complete. We have shown elsewhere[5,6] that isometric recording is a most sensitive method for block detection, and the present study suggests that impairment in the bulk transfer of cerebrospinal fluid during the Queckenstedt maneuver is the major factor in causing prolonged pressure rise (and fall) times.

The execution of a Queckenstedt test under fluoroscopy should be a useful adjunct to myelography in any patient not previously subjected to precise manometric studies. If a rapid movement of contrast medium is observed in the upper lumbar canal on jugular compression, the radiologist will know even before passing the contrast material in the cranial direction, that no gross obstruction is to be expected. On the other hand, if the contrast medium

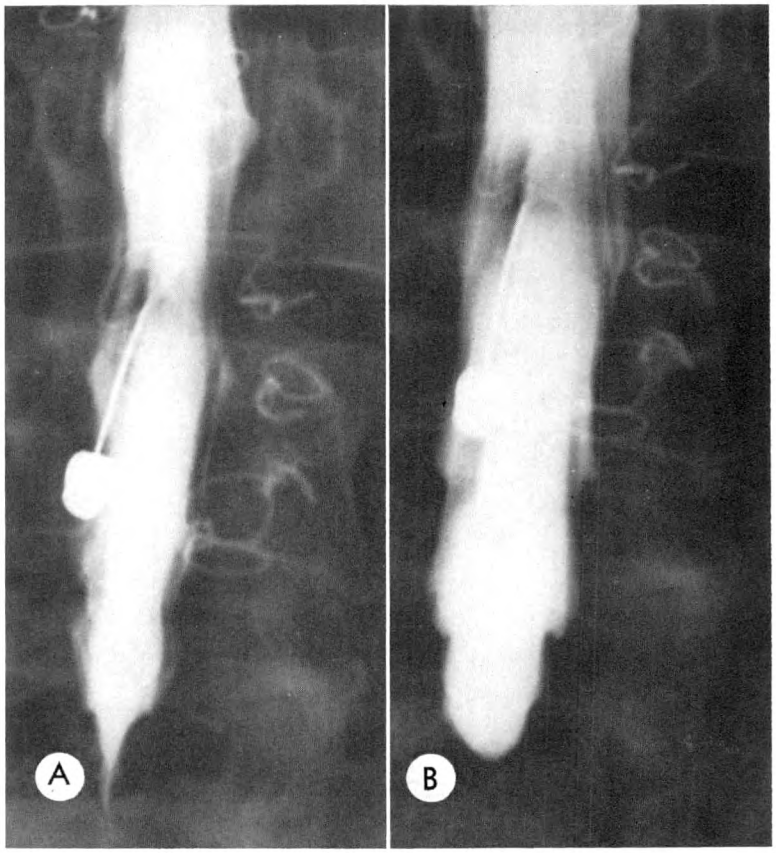


FIG. 2. (*A*) The lumbar sac before compression, and (*B*) the distended sac about 3 seconds after initiation of sustained compression. Note the increased transverse diameter.

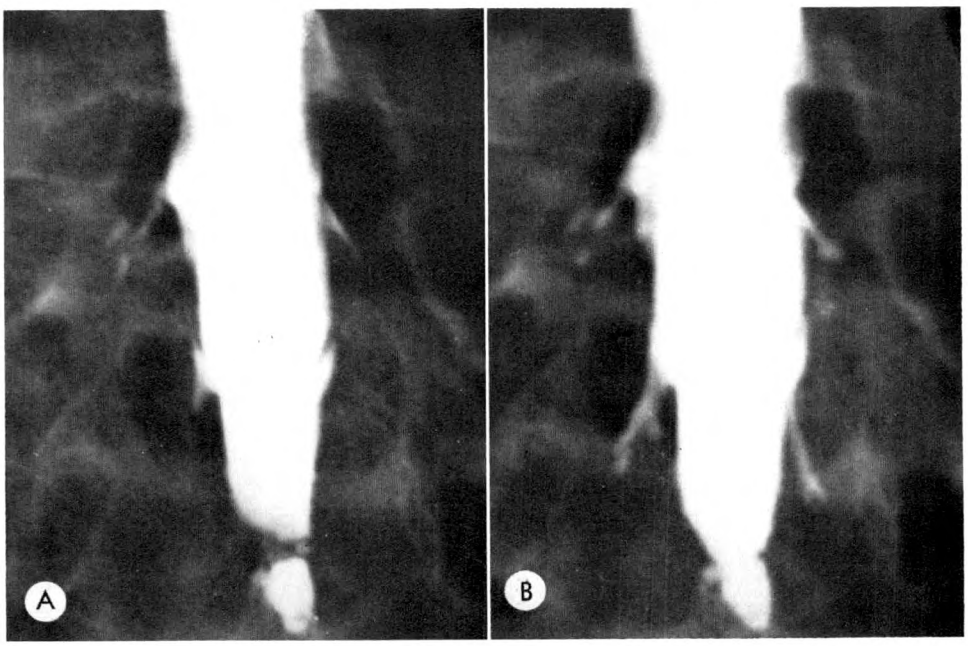


FIG. 3. Case 6. (*A* and *B*) The lumbar sac before and after approximately 3 seconds of sustained jugular compression. Note that the contrast medium has been forced into the root sleeves.

movement is slow, this will indicate an obstruction, and the information will assist in the further planning of the myelographic procedure. It should be emphasized, however, that the jugular compression has to be promptly instituted with application of a brisk force over the sternocleidomastoid muscles. Obviously the carotid sinus should not be touched, as bradycardia adversely affects the response.[5] The appropriate technique can be easily mastered with minimal practice. It should also be ascertained that the patient does not strain or hold his breath, as this will increase abdominal pressure, which in turn will cause engorgement of the lower spinal venous plexus, counteracting the downward cerebrospinal fluid flow.

SUMMARY

As an adjunct to routine pantopaque myelographic studies in 8 patients, cinemyelographic studies were made of the contrast medium movement on prompt jugular compression (Queckenstedt test). Isometric lumbar cerebrospinal fluid manometric studies were simultaneously performed, using a new strain gauge minitransducer, linked with a direct writing recorder.

It was found that jugular compression displaced the contrast material 3 to 5 vertebral bodies caudally within 0.5 seconds. Maximum contrast medium flow velocity in the cervical and thoracic area varied between 9 and 43 cm. per second. In the lower lumbar canal there was no caudal shift, but a marked distention of the sac, with an approximately 40 per cent increase in lateral diameter. The jugular compression also brought about improved visualization of the root sleeves by contrast medium filling.

The findings confirm assumptions made on the basis of isometric manometrics, that the Queckenstedt maneuver normally induces a rapid and marked downward bulk shift of spinal fluid. Previous opinions on the dynamics and adequacy of open-end manometric studies are refuted by the present observations.

The diagnostic value of performing the Queckenstedt test at the time of myelography is emphasized, both for the evaluation of existing obstructions and the visualization of lumbar root sleeves.

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CAROTID CAVERNOUS FISTULA PRESENTING AS A NASOPHARYNGEAL MASS*

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AN ARTIFICIAL communication between the intracavernous portion of the internal carotid artery and the surrounding venous plexuses within the carotid sinus may produce a characteristic syndrome comprised of severe unilateral headache accompanied by homolateral carotid bruit, progressive exophthalmos with edema and retinal hemorrhages, and variable degrees of ophthalmoplegia followed by subsequent blindness.

The paired cavernous sinuses and their contents, consisting of the internal carotid arteries, the third, fourth and sixth cranial nerves and the ophthalmic division of the fifth nerve, rest on the lateral aspects of the body of the sphenoid bone and are vulnerable to injury either of the direct penetrating type, *e.g.*, gunshot wounds, or of the indirect, nonpenetrating variety, *e.g.*, basilar skull fractures. Approximately 75 per cent of carotid cavernous fistulas occur secondary to trauma, whereas the remaining 25 per cent appear to originate spontaneously from rupture of a previously diseased arterial wall.[1]

Once the fistula has been created, unless thrombosis intervenes, there is usually enlargement of the cavernous sinus which may lead by pressure erosion to expansion or rupture into the sphenoid sinuses. Fatal hemorrhage has been observed as a consequence of the latter.[2]

The purpose of this paper is to document a further complication, believed previously unreported, of further expansion of a fistula through the anterior aspect of the body of the sphenoid bone into the nasopharynx. The venous drainage, which was somewhat unusual, will be briefly discussed.

REPORT OF A CASE

A 26 year old man was admitted to this hospital with a 2 year history of nasal stuffiness, anosmia and rhinorrhea unrelieved by antihistamines. Four years prior to admission, while in military service, he had fallen 30 feet from the deck of a ship onto a steel pier sustaining fractures of the cranial vault, facial bones and left femur. His right tympanic membrane was perforated. He regained consciousness 6 weeks after the multiple injuries but was totally blind in the left eye and had only light perception remaining on the right. He could not recall experiencing headache or vertigo.

On physical examination, the patient was well developed, well nourished and in no apparent distress. Blood pressure was 120/80.

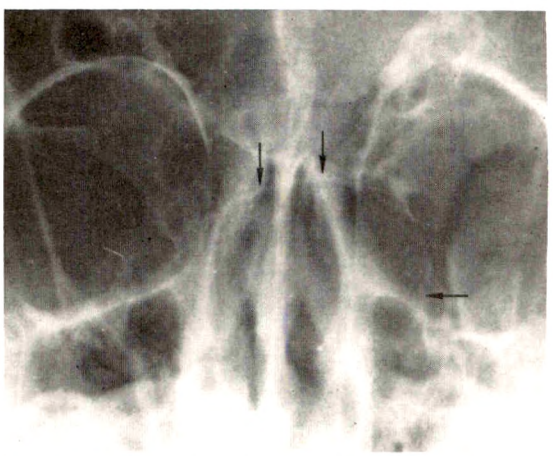


FIG. 1. Waters' view. A large, relatively radiolucent mass is superimposed on the nasal cavity and intrudes into the left orbit. Note the thin calcific or bone rim (arrows). On the left there is also narrowing and lateral displacement of the inferior aspect of the superior orbital fissure and elevation and flattening of the optic foramen. The lesser and greater sphenoidal wings appear demineralized. Some hazy opacification of the left frontal sinus and ethmoidal air cells is present.

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Pertinent findings included slightly decreased hearing on the right, bilateral optic atrophy with light perception only in the right temporal field, extra-ocular muscle palsies and anosmia. A large, rubbery, nonpulsatile mass covered by mucosa was obstructing the left nares and appeared to extend posteriorly into the nasopharynx. This was thought to represent a large nasal polyp and was biopsied. The latter procedure was accompanied by extensive hemorrhage with an estimated blood loss of 2,000 cc. After hemostasis was obtained with anterior and posterior nasal packs, the patient was transfused and transferred to neurosurgery. At this time a bruit was heard over the left eye. Bilateral carotid arteriography disclosed a massive carotid cavernous fistula which was surgically treated by muscle embolization. A temporalis fascia graft was used to repair the cranionasal fistula. The patient did well postoperatively but did not regain vision.

DISCUSSION

The primarily intracranial nature of the pathology in this patient was initially masked by his upper respiratory complaints, despite certain historical and clinical features compatible with the carotid cavernous syndrome. It would appear most likely that the precipitating event was a basilar skull fracture in the region of, or directly involving, the basisphenoid with laceration of the intracavernous portion of the internal carotid artery.

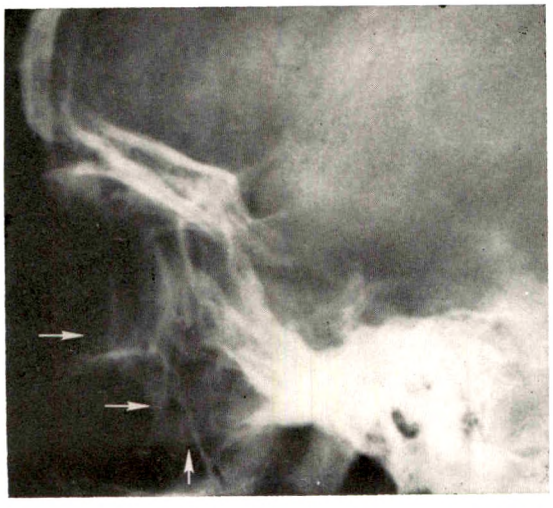


Fig. 2. Lateral view. The destruction of the sella turcica and sphenoid sinuses is obvious. A soft tissue mass is superimposed on the posterior pharynx and maxillary antra as well as the posterior portion of the orbits (arrows).

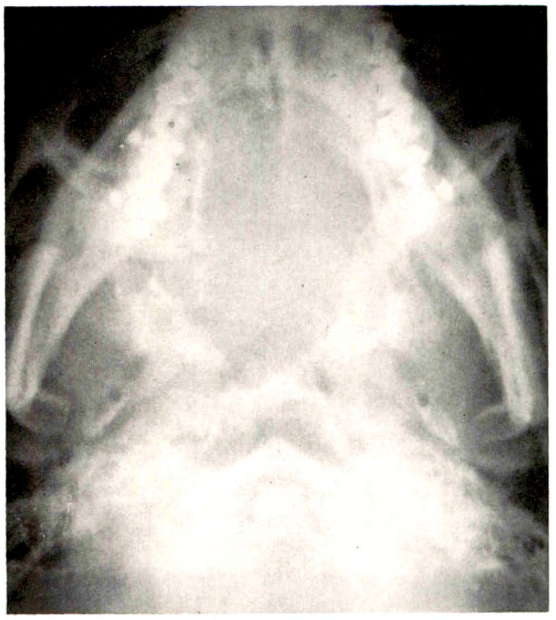


Fig. 3. Submentovertex projection. A large area of excavation extends from the region of the posterior clinoids well into the anterior cranial fossa.

Shortly after admission, paranasal sinus roentgenograms were obtained and a large medial calcific or bone rimmed mass was seen to extend from the nasopharynx to the middle fossa (Fig. 1 and 2), displacing and eroding contiguous structures. The extent of the basilar destructive change was best visualized in the submentovertex projection, which disclosed central excavation of both middle and anterior fossae (Fig. 3). Further anatomic detail delineated with laminagraphy, utilizing a hypocycloidal trajectory (Fig. 4, *A* and *B*) provided evidence that the lesion was expansile rather than invasive.

The lateral displacement of the inferior aspect of the left superior orbital fissure, erosion of the greater and lesser sphenoidal wings on the left, and anterior and middle fossae destruction were thought to represent changes compatible with infraclinoid aneurysm, marked extrasellar extension of a pituitary tumor, and chordoma or muco-

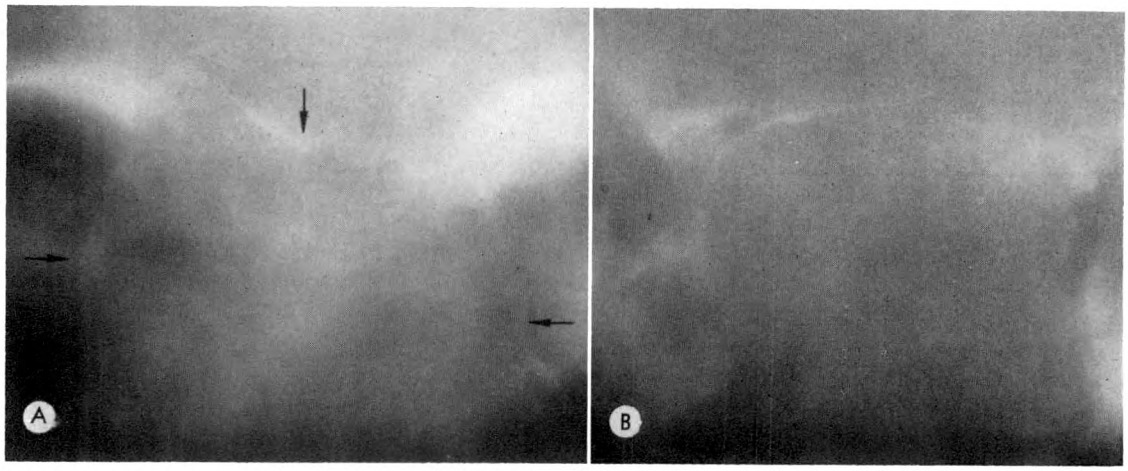


FIG. 4. (*A*) Laminagraphy through the coronal plane of the posterior orbits. Note fragmentation and expansion of the planum sphenoidale (upper arrow) and intrusion of a mass into the medial aspect of both orbits (lateral arrows). (*B*) Laminagram 1 cm. posterior to *A*. The mass appears symmetric at this level. The tuberculum sellae is elevated and both anterior clinoids are laterally displaced.

cele of the sphenoid sinus. The possibility of a meningioma was also entertained, since certain of the roentgen findings were similar to those reported by Rischbieth and Bull.[4] In a series of 102 cases of pterional, sphenoid wing and middle fossa meningiomata

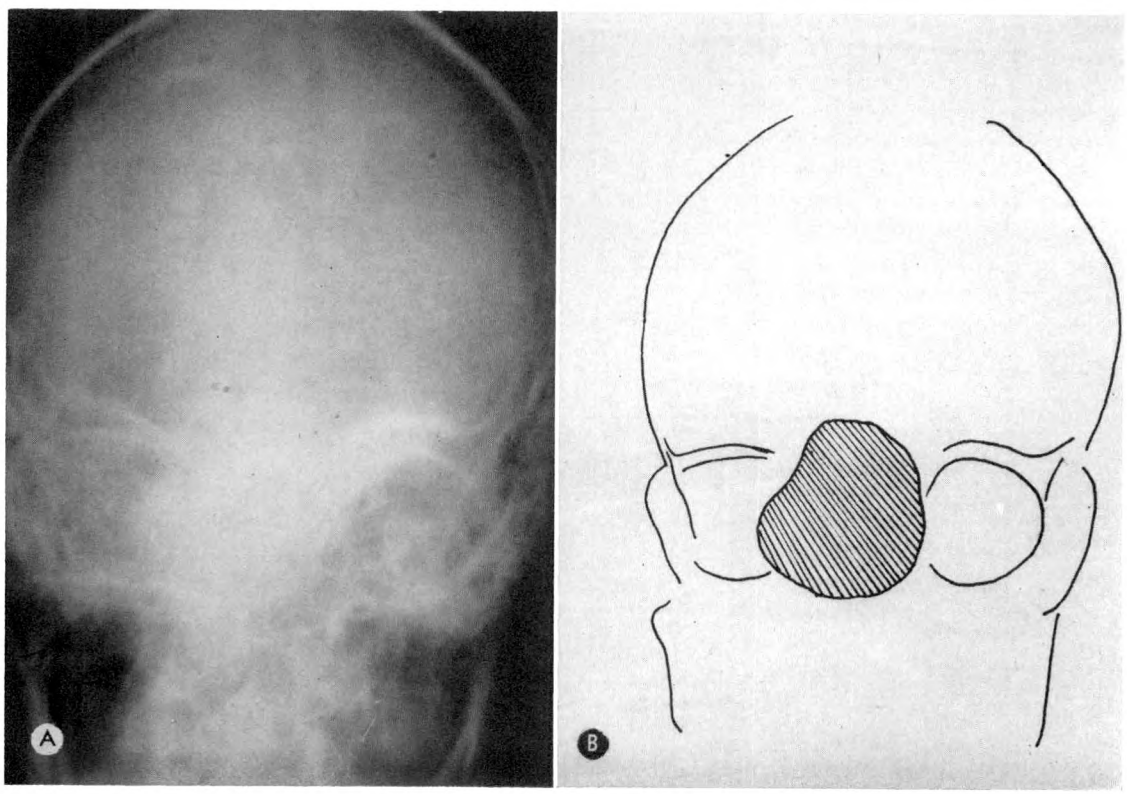


FIG. 5. (*A*) Internal carotid arteriogram, frontal projection. Film was exposed 2 seconds after injection. Contrast material fills the mass. (*B*) Diagram indicates area of opacification.

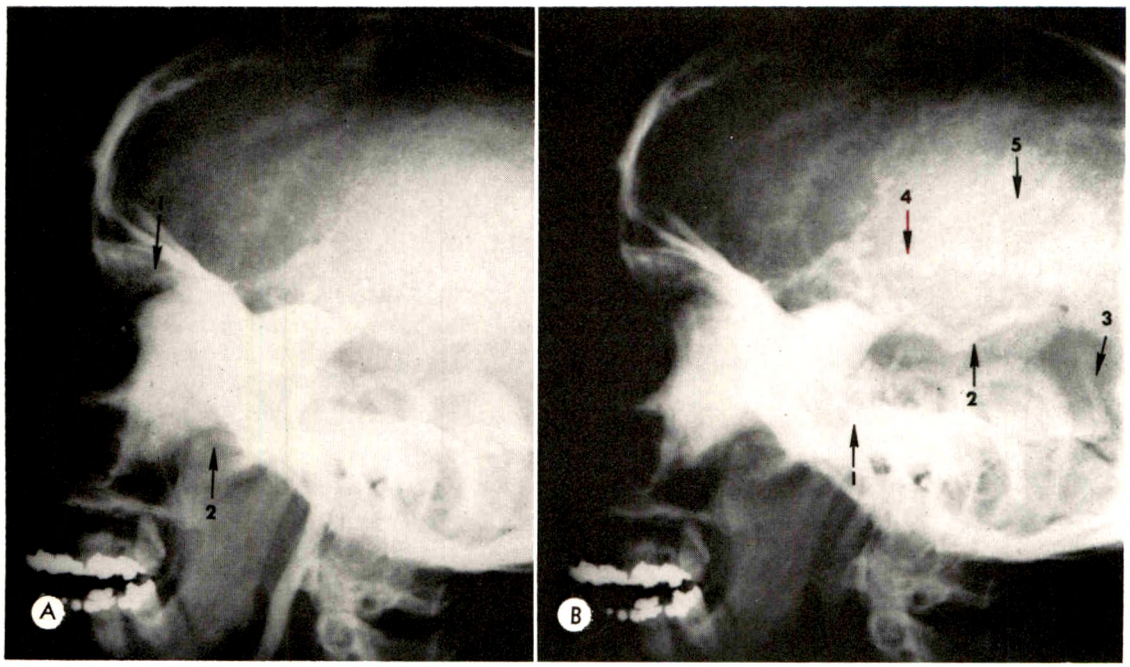


Fig. 6. (*A*) Internal carotid arteriogram, lateral projection. Film was exposed 2 seconds after injection. An arterial venous communication at the level of the cavernous sinus is evident. Several enlarged veins draining into the pterygoid plexus (2) are shown, but the ophthalmic vein (1) is small. There is sparse filling of a few branches of the middle cerebral artery. (*B*) Internal carotid arteriogram, lateral projection. Film was exposed 4 seconds after injection. The route of venous drainage is via deep and superficial intracerebral veins: (1) basilar plexus with faint contrast outlining the superior and inferior petrosal sinuses; (2) basilar vein; (3) straight sinus; (4) superficial middle cerebral vein (sylvian); and (5) great anastomotic vein of Trolard.

they described 4 cases in which the classic bone sclerosis was not present and demineralization and displacement of adjacent structures predominated.

Total opacification of the mass immediately following selective positive contrast medium injection into the left internal carotid artery (Fig. 5, *A* and *B*; and 6*A*) unequivocally established the existence of a carotid cavernous fistula. Right carotid arteriography with contralateral common carotid pressure did not disclose any apparent vascular contribution to the fistula from the right anterior cerebral circulation.

The absence clinically of exophthalmos either of the pulsatile or nonpulsatile type was assumed attributable to the release of retro-orbital pressure through the cranionasal fistula and lack of significant drainage through the ophthalmic venous pathway (Fig. 6*B*).

Dilatation of the superior ophthalmic veins, which commonly occurs in response to increased pressure within the cavernous sinus, is a result of a relative lack of resistance in venous structures which lack valves and are poorly supported by surrounding tissues. Conversely, the dura encasing the intracranial sinuses is rigid and relatively unyielding to pressure changes. In general, therefore, in the presence of marked spasm or thrombosis of the ophthalmic veins, drainage is primarily through the cortical veins. In 1939, Wolff and Schmid[5] outlined 6 routes of venous drainage in carotid cavernous fistulas, 4 of which occur primarily through the dural sinuses, or convexity veins and dural sinuses, and 2 routes following the more usual ophthalmic drainage. More recently, Clemens and Lodin[3] expressed the opinion that the type of predominant outflow

channel is probably a function of the kind of trauma, site of fracture and fistula size, in addition to being influenced by the anatomic variations of the cavernous sinus.

SUMMARY

A massive carotid cavernous fistula which eroded into the nasopharynx creating a cranionasal fistula and presented clinically as a nasopharyngeal mass is reported.

The roentgenographic changes, most markedly involving the sphenoid bone, and uncommon venous drainage of the fistula are discussed.

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The authors wish to express appreciation to Dr. Sanford Larson, Chairman of the Department of Neurosurgery, Marquette School of Medicine, for cooperation in assembling the clinical material.

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INTRATHORACIC MENINGOCELE*

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AN INTRATHORACIC meningocele is a saccular protrusion of the dural sac through an enlarged intravertebral foramen; it projects paravertebrally into the thoracic cavity, displacing the posterior pleura. Seventy per cent of the intrathoracic meningoceles reported in the literature occurred in patients with neurofibromatosis.[1,3,8–11] The posterior mediastinal mass observed in the survey chest roentgenograms is often erroneously interpreted as neurofibroma.

The purpose of this paper is to emphasize this entity and to present a case report.

REPORT OF A CASE

An asymptomatic 44 year old woman was admitted to the Jefferson Medical College Hospital because of an abnormal survey chest roentgenogram. The systemic review disclosed no abnormalities. The patient was a nonsmoker. There was no family history of neurofibromatosis, skin tumors or café au lait spots. A slight bilateral hearing loss was of undetermined etiology.

The results of laboratory studies were within normal limits. Skull roentgenograms revealed no abnormalities. An examination of the chest disclosed a large mass in the posterior mediastinum with multiple scalloped erosions of the upper thoracic vertebrae (Fig. 1, *A*, *B* and *C*). The mass was initially thought to be a neurofibroma.

A thoracic myelogram showed the opaque medium filling the large mass noted on the roentgenograms. Several small meningoceles not identified on the survey roentgenograms also filled with the opaque material (Fig. 2, *A* and *B*). The rest of the subarachnoid space was normal. Fluoroscopy and cine studies revealed no pulsations in the intrathoracic meningocele.

No treatment was administered because of the absence of symptoms, and the patient was discharged, to be followed by serial chest roentgenography. No change had been noted after $6\frac{1}{2}$ months, at the time of this report.

DISCUSSION

The first case of intrathoracic meningocele was reported by Pohl[12] in 1933. The etiology has not been established. The meningocele is probably the result of a neural arch derangement with herniation of meningeal structures through the defect. Constant pulsations may erode the bone progressively.[2,7,13]

Intrathoracic meningoceles have been found in patients from 2 days to 68 years of age.[3] Most of them are discovered in the fourth and fifth decades. There is no sex predominance.[1,8,14]

The majority of intrathoracic meningoceles present on the right side, and less than 10 per cent are bilateral.[8,14]

Intrathoracic meningoceles which pulsate may enlarge over a period of 2 to 11 years,[1,2] while those which do not pulsate may not change in size or shape. One would expect meningoceles to reflect the pulsations of the subarachnoid space;[4] however, Byron *et al.*[2] reported a meningocele which did not pulsate and did not enlarge in a 2 year period. Unfortunately, myelography was not performed, and the mediastinal mass was believed to be an intrathoracic neurofibroma. Uncontrollable bleeding during thoracotomy led to the patient's death. Autopsy revealed a meningocele adherent to the surrounding pleura, vertebral bodies and ribs, which explained the lack of pulsation. We believe that the lack of pulsation is a reliable sign of stability.

The meningocele in our patient did not pulsate or respond to the Valsalva and Müller maneuvers in spite of direct communication with the subarachnoid space, and we concluded that it was stable because of fibrous tissue formation peripherally. No change in size of the lesion was noted during 6 months of observation.

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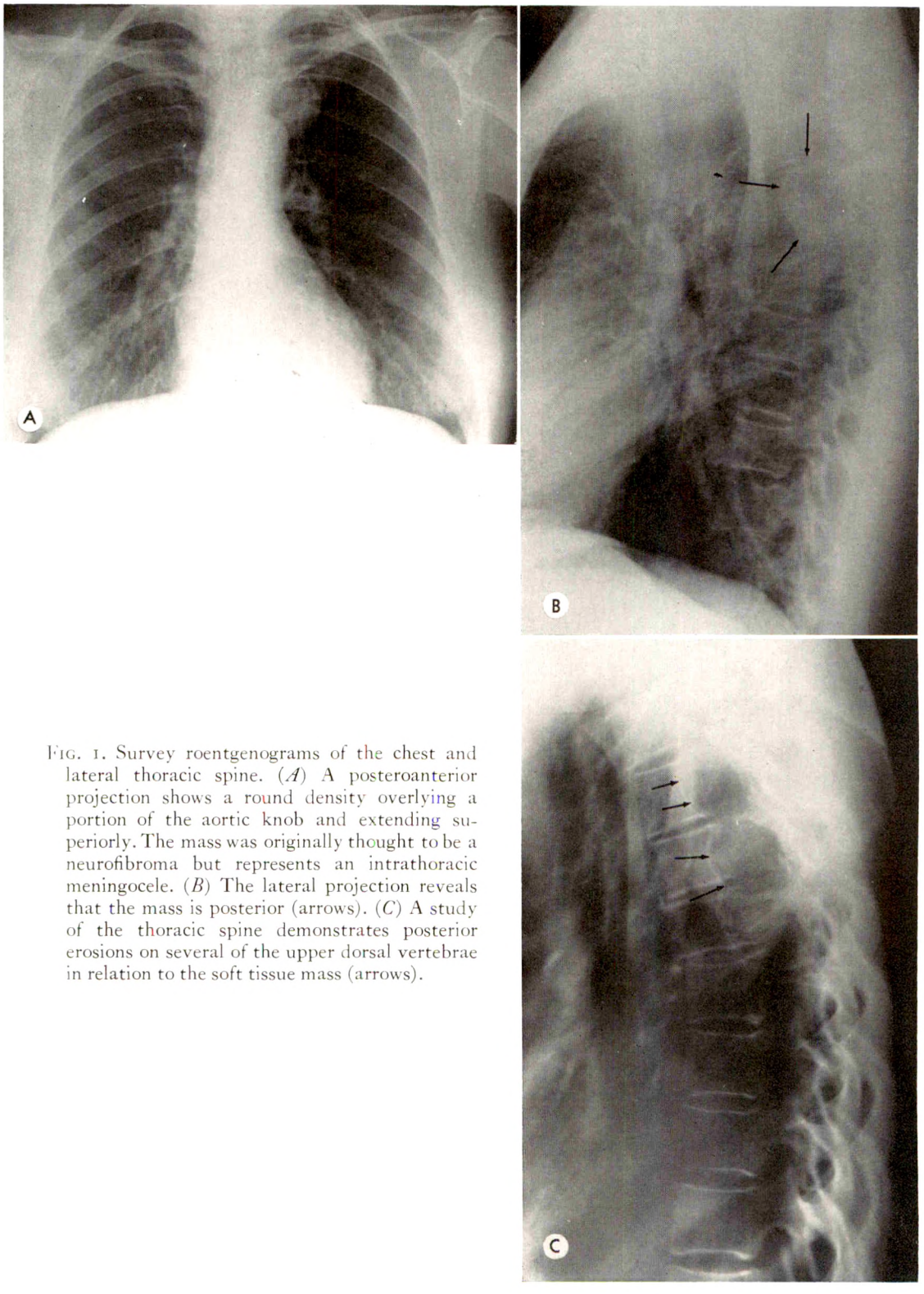


FIG. 1. Survey roentgenograms of the chest and lateral thoracic spine. (*A*) A posteroanterior projection shows a round density overlying a portion of the aortic knob and extending superiorly. The mass was originally thought to be a neurofibroma but represents an intrathoracic meningocele. (*B*) The lateral projection reveals that the mass is posterior (arrows). (*C*) A study of the thoracic spine demonstrates posterior erosions on several of the upper dorsal vertebrae in relation to the soft tissue mass (arrows).

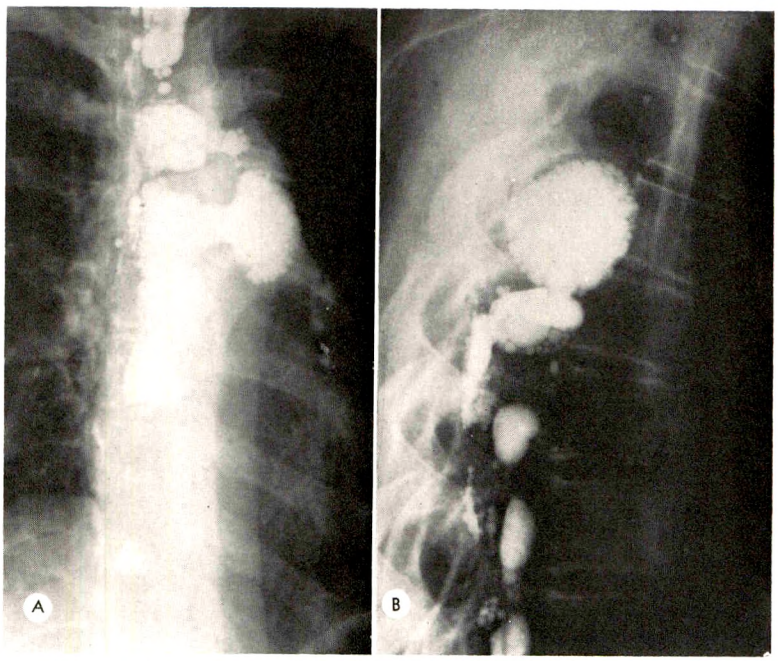


Fig. 2. (*A*) Anteroposterior and (*B*) lateral roentgenograms taken during myelography reveal the direct communication of the meningocele to the subarachnoid space. Several small meningoceles are located above and below the largest one. The meningoceles are not completely filled.

Patients with lateral meningocele are usually free from neurologic symptoms. Occasionally, pressure on adjacent structures causes pain. In contrast, neurofibroma commonly produces neurologic signs and symptoms, the result of the intraspinal component which affects the spinal cord and nerve roots.[8,10,11] Pain may also result from pressure on the intercostal nerves.

A mediastinal mass in a patient with neurofibromatosis is more often a meningocele than a neurofibroma.

The roentgen features of meningoceles are: intravertebral foramina enlargement, pedicle erosion, increase of interpediculate measurements, dorsal erosion of vertebral centra and well defined paravertebral soft tissue mass. Since neurofibroma and meningocele cysts have similar roentgenographic characteristics,[3,5,6] myelography is essential for roentgenologic diagnosis.

TREATMENT

Surgery is to be avoided unless there are progressive manifestations or growth of a meningocele. Postoperative spinal fluid fistula is a common complication; the larger the meningocele, the greater the incidence of the complication. Lack of pulsations of a meningocele suggests an adequate fibrous capsule or adhesion which should prevent progressive growth and symptoms.

Some workers advocate early surgical intervention, in the absence of symptoms, in view of the fact that these meningoceles may grow progressively, with increasing risk.[14] We believe, however, that in asymptomatic patients, surgery is contraindicated if a meningocele is non-pulsating. Progressive enlargement of the mass, symptoms and bone erosion are indications for surgery.

SUMMARY

1. A case of intrathoracic meningocele is reported with a brief review of the literature.

2. Fluoroscopic and cine roentgenologic studies failed to demonstrate pulsations or change in size of the lateral meningocele. These findings are believed to be evidence

of stability resulting from peripheral fibrosis.

3. No change was noted in the patient reported herein 6½ months after the diagnosis was made.

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Vol. 106, No. 2

INITIAL HIGH DOSE IRRADIATION FOR METASTASES CAUSING SPINAL CORD COMPRESSION IN CHILDREN*

By M. TEFFT, M.D.,† ANNA MITUS, M.D.,‡ *and* M. D. SCHULZ, M.D.§
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EXTRADURAL metastasis with compression of the spinal cord is not a common complication of the malignancies of childhood. When it does occur, it can be most distressing, both to patient and family, and constitutes a radiotherapeutic or surgical emergency to obtain regression of signs and symptoms and thus to retain viability of the spinal cord.

Since 1963, we decided to evaluate the role of initial high dose radiotherapy in children who had a radiosensitive neoplasm which had metastasized to the area around the spinal cord, who had evidence of widespread metastatic disease, whose clinical condition made a surgical procedure less than desirable, and/or who had either noncontiguous multiple sites of spinal cord compression or involvement of a large segment of the spinal cord. With this radiotherapeutic approach we hoped for rapid and complete resolution of the signs and symptoms due to spinal cord compression. However, our experience is limited due to the infrequency of the problem in children.

Six children have been admitted within the past 5 years with the complication of spinal cord compression. All had metastatic involvement of the tissues about the cord. Each child had a lesion which either had shown response to irradiation prior to the onset of the clinical picture of cord compression or one that was known to be responsive.

REPORT OF CASES

CASE 1. K. W., a 9 year old boy, was admitted to the Massachusetts General Hospital in June, 1960, with a 2 week history of headache, lethargy and vomiting. Positive physical examination findings were bilateral diplopia on lateral gaze and vertical nystagmus on upward gaze. The pupils reacted sluggishly to light but better to accomodation.

Air ventriculography and contrast arteriography revealed a mass lesion in the region of the pineal gland. A tentative diagnosis of pinealoma was made; because of the location, biopsy was contraindicated.

He was treated with a Torkildson shunt to relieve the internal hydrocephalus and was referred for irradiation.

Radiation therapy consisting of 2,100 rads of cobalt 60 through opposed lateral portals and 2,400 rads with 2 mev. Van de Graaf using 360° rotation for a total of 4,500 rads was delivered to the pineal mass in 35 elapsed days. Following the completion of irradiation, his signs and symptoms were no longer apparent. A repeat roentgenographic contrast medium examination was not performed to document regression of the lesion.

He was well until December, 1961, when he developed a large soft tissue mass overlying the proximal right femur. Roentgenograms revealed osteolytic destruction of the proximal right femur; in addition, the fourth lumbar vertebral body showed slight compression. Biopsy of the soft tissue mass was consistent with metastatic pinealoma. Assay of the tissue for hydroxyindole-O-methyl transferase indicated increased enzyme activity.

Radiation therapy consisting of 2,000 rads in 11 elapsed days at 200 rads per day; 280 kvp., 19 ma., half-value layer 3.4 mm. Cu, was delivered to each of the involved areas. His symptoms improved, the pain in the right femur diminished and mobility of the right leg increased subsequently. Marked regression of the soft tissue mass was observed at the end of this course of therapy.

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiology (Division of Radiotherapy) of the Children's Hospital Medical Center,† the Department of Radiology (Radiotherapy), the Massachusetts General Hospital,§ the Children's Cancer Research Foundation;‡ and from the Department of Radiology,†§ and Pediatrics‡ of the Harvard Medical School, Boston, Massachusetts.

TABLE I

LOW INITIAL DOSE THERAPY FOR EXTRADURAL METASTASES

Case I	Symptoms Prior to Therapy	Radiation Therapy		Result
	Paraplegia, incontinence	Day 1		
		A.M.	25 rads	Complete resolution of spinal cord compression beginning at 1 week after therapy
		P.M.	50 rads	
		Day 2		
		A.M.	50 rads	
		P.M.	50 rads	
		Day 3 etc.	200 rads	

He remained well until January, 1962, when paraplegia and bowel and bladder incontinence occurred suddenly. Roentgenograms demonstrated destruction and compression of the fourth and fifth thoracic vertebral bodies due to metastases. There was an associated paraspinal mass.

Radiation therapy was directed to the area of T-3 to T-9 vertebral bodies and associated paraspinal region. Small initial doses were delivered (Table 1). A total of 2,150 rads (2 mev. Van de Graaf) in 14 elapsed days resulted in slow and gradual improvement, control of both bowel and bladder function and ability to voluntarily move both lower extremities. No worsening of his clinical symptoms occurred during the course of irradiation.

In April, 1962, he developed sudden severe pain associated with marked local tenderness in the upper lumbar area. There was a firm and tender mass in the subcutaneous tissues of the posterior chest wall, to the left of the first lumbar vertebral body.

Radiation therapy was delivered to the lumbar spine and paravertebral mass. Two hundred rads (280 kvp., 19 ma., half-value layer 3.4 mm. Cu) per day, including the initial dose, was delivered without untoward event to a total dose of 1,000 rads in 6 elapsed days. By this time, complete regression of both pain and the palpable mass had occurred.

During the ensuing 20 months, he developed several manifestations of metastases in both the skeletal system and the peripheral lung fields. These were each treated with similar palliative doses of irradiation and both subjective and objective improvement occurred.

In December, 1963, he developed spasm and stiffness of the right leg and pain along the lumbar spine. Tenderness in the lower lumbar spine and resistance to straight leg raising were noted at physical examination. Radiation therapy (280 kvp., 19 ma., half-value layer 3.4 mm. Cu) was delivered to the spinal column from the levels of T-10 to L-5. A total dose of 1,450 rads in 9 elapsed days was delivered at a dose rate of 200 rads per day, including the initial dose. No adverse reaction occurred during his course of irradiation. Stiffness and pain in the lower extremities had disappeared by the time of completion of irradiation.

Within 1 month, however, he developed recurrent back pain, constipation followed by fecal and urinary incontinence, and paresthesias followed by loss of sensation of his lower extremities. These symptoms developed over a 3 week period; the symptoms of more severe spinal cord involvement occurred over a 24 to 48 hour period. At physical examination on this admission, he showed less ability to straighten his legs than on previous examinations and slight tenderness over the spinous processes of vertebral bodies T-3 through T-5. There was spasticity of both lower extremities, the right greater than the left. Diminished deep tendon reflexes were observed in lower extremities but were normal in upper extremities; there was marked ankle and plantar clonus, abdominal and cremasteric muscle reflexes were absent, and both Babinski reflexes were positive. All sensation over the lower half of his body was diminished; a sensory level was placed at T-7.

Three days later he developed sudden paraplegia. Deep tendon reflexes were 4+ on the

TABLE II

HIGH INITIAL DOSE THERAPY FOR EXTRADURAL METASTASES

SUMMARY OF CASES

Case	Diagnosis	Symptoms (duration)	Signs Before Start of Treatment		Laboratory Findings	Radiation Therapy	Results (day of radiation therapy)
			Clinical	Roentgen			
I	Pinealoma	Back pain (3 wk.); incontinence (1 wk.); paresthesias (1 wk.); paraplegia (24 hr.)	Tenderness T-3–T-5; loss of motor power (lower extremities); spasticity (lower extremities); clonus (ankle, plantar); absent abdominal and cremasteric reflexes; deep tendon reflexes 3+ lower extremities; positive bilateral Babinski sign; loss of sensation below T-5	Multiple vertebral metastases in thoracic and lumbar spine	Cerebrospinal fluid protein 970 mg. per cent	Day 1: 500 rads Day 2: 500 rads Day 3: 500 rads Day 4: 200 rads	Day 1: decrease in sensory loss at 6 hr. Day 4: sensation regained below T-5; sphincter control; voluntary movement in lower extremities Day 14: 1+ symmetric reflexes; negative Babinski sign
II	Ewing's sarcoma	Low back pain (3 wk.); ataxia (3 d.)	Deep tendon reflex 3+ in lower extremities; bilateral positive Babinski sign	Myelogram; block at T-11 and T-12	Cerebrospinal fluid protein 97 mg. per cent	Day 1: 750 rads Day 2: 750 rads Day 3: 200 rads etc. (See text)	Day 2: deep tendon reflex 2+ Day 3: block resolved by myelogram Day 30: absent back pain; no ataxia; deep tendon reflex 1+; negative Babinski sign
III	Wilms' tumor	Back pain (24 hr.); incontinent (24 hr.); paraplegia (12 hr.)	Deep tendon reflexes 3–4+ lower extremities; bilateral positive Babinski sign	Multiple lesions of vertebral bodies of thoracic spine; myelogram: block at C-7–T-1 level		Day 1: 750 rads Day 2: 750 rads Day 3: 200 rads	Day 3: pain relief Day 7: sphincter control; movement of lower extremity
IV	Atypical pinealoma	Back pain (3 wk.); inability to void (24 hr.); diminished motor power of lower extremities (24 hr.)	Deep tendon reflexes 3+ of lower extremity, hypoesthesia below T-6	Myelogram: block at L-2 and T-5; multiple defects in contrast medium column		Day 1: 750 rads (T-5–L-5) Day 2: 750 rads (T-5–L-5) 300 rads (C-1–T-4) Day 3: 150 rads (C-1–L-5) etc. (see text)	Day 1: sensory level at T-4 Day 2: sensory level at T-6 Day 3: sensation normal; deep tendon reflexes 1+; sphincter control
V	Neuroblastoma	Paraplegia (5 d); sensory level at T-3 (48 hr.); incontinent (48 hr.)	Absent deep tendon reflexes lower extremities; sensory level at T-3; bilateral+Babinski sign	Multiple thoracic-lumbar vertebral body destruction		Day 1: 750 rads Day 2: 750 rads Day 3: 500 rads	Day 2: right foot moved voluntarily Day 3: sensation regained Day 5: sphincter control
VI	Neuroblastoma	Back pain (2 wk.); weakness lower extremities (3 d.); unable to urinate (3 d.); back pain (3 d.)	Deep tendon reflexes 3+ lower extremities; tenderness (T-9); bilateral +Babinski sign; deep tendon reflexes 3+ lower extremities; paraplegia; right ankle clonus	Myelogram: block at T-11–T-12	Cerebrospinal fluid protein 67 mg. per cent	Day 1: 400 rads Day 2: 400 rads Day 3: 400 rads Day 4: 400 rads Day 1: 1,000 rads Day 2: 500 rads	All symptoms and signs regressed at 1 wk. Day 1: pain improved at 6 hr. Day 2: sensation normal Day 3: moved lower extremities Day 5: sphincter controlled; myelogram-block resolved

right and 3+ on the left lower extremity; ankle clonus and positive Babinski signs were present bilaterally. His sensory level was now at T-5.

Solumedrol was administered (20 mg. intramuscularly and 40 mg. every 6 hours). Irradiation began simultaneously, 500 rads (Co^{60}, half-value layer 12 mm. Cu) was delivered to the spinal cord from the level of T-4 to T-8, using a single 8×5 cm. posterior portal. Within 12 hours, he noted an increase in sensation to pain and light touch down to the level of the third lumbar segment. A myelogram at this time revealed a complete block to the free flow of contrast material at the level of T-7. Cerebrospinal fluid protein determination was 970 mg. per cent.

He received an additional 500 rads on each of the next 2 successive days and a final dose of 250 rads on the fourth treatment day for a total dose of 1,750 rads in 5 elapsed days (Table II).

By the fourth treatment day he had regained sensation and voluntary movement in the lower extremities, and had regained control of both bowel and bladder functions.

Within 2 weeks of the completion of therapy, his reflexes were 1+ and symmetrical throughout and his Babinski response was negative.

He remains alive and relatively well at this time under treatment with local irradiation on occasion for palliation and with chemotherapy.

CASE II. J. C., a $3\frac{1}{2}$ year old boy, was admitted to the Children's Hospital Medical Center in June, 1964, because of pain in the left leg. Slight swelling was present over the medial and proximal left tibia. Roentgenography revealed an osteolytic destructive lesion of the left tibia. Biopsy confirmed the impression of Ewing's sarcoma. Radiation therapy (250 kvp., 15 ma., Th 2 filter, half-value layer 2.6 mm. Cu) was delivered to the entire shaft of the left tibia to a dose of 6,000 rads in 42 days using 340° arc rotation.

He remained well until August, 1965, when he developed low back pain which radiated to the right flank, right inguinal region and right lower abdomen. This progressed over a 3 week period. The pain increased over the last 3 days of this period and he developed ataxia. He noted no paresthesia or radiation of the pain into the lower extremities.

Physical examination revealed an ataxic gait. Sensation was intact throughout and he had good coordination of upper and lower extremities. Deep tendon reflexes were increased slightly in the lower extremities (2+ to 3+) and bilateral positive Babinski reflexes were elicited. No clonus was present.

Lumbar puncture showed normal manometric pressure but the spinal fluid protein was 97 mg. per cent. Myelography revealed an apparent complete block to the free flow of contrast medium at the T-11–T-12 interspace. The contrast material was not removed.[5] He was treated with Decadron (0.1 mg. per pound body weight by mouth every 24 hours) and irradiation consisting of 750 rads delivered from the level of T-9 to L-1 through single 9×5 cm. posterior portal. This was repeated at 24 hours. On the third day the dose was reduced to 200 rads daily fractions.

Twenty-four hours after his first treatment, his reflexes were slightly less active (2+). By the fourth day of irradiation, repeat fluoroscopy of contrast material retained in the spinal column revealed complete resolution of the block. His symptoms of ataxic gait and back pain abated gradually over the ensuing weeks and his reflexes returned to normal. A total dose of 4,500 rads in 21 elapsed days was delivered.

He remained well until February, 1966, when he developed recurrence of spinal "cord" symptoms, abdominal pain and severe dysesthesia. A mass over the right frontal bone was biopsied and was consistent with metastatic Ewing's sarcoma. He received palliative irradiation to the paraspinal area (direct irradiation of the previously treated spinal cord was avoided by the use of a 3 mm. Pb cord block) and to the right frontal bone. Relief of spinal cord symptoms was noted within 2 days and the right frontal mass regressed within 1 week. A dose of 1,800 rads in 12 elapsed days was delivered to each area.

Thereafter he developed widespread metastases and died in December, 1967.

CASE III. L. B., a $1\frac{1}{2}$ year old child, had a left Wilms' tumor removed in June, 1964. Postoperatively, she received irradiation (2,000 rads in 2 weeks; 250 kvp., 15 ma., half-value layer 2.8 mm. Cu) to the left renal fossa and concomitant chemotherapy.

She remained well until March, 1965, when she developed pain and swelling about the left wrist. Roentgenography revealed a destructive lesion of the distal left radius with pathologic fracture. This was treated with radiation therapy consisting of 2,400 rads in 3 treatments administered with the orthovoltage technique (same factors as in June, 1964).

In June, 1965, a mass appeared overlying the right zygoma. There was associated destruction of underlying bone. She was referred to the Children's Hospital Medical Center where chemotherapy was begun and she received radiation therapy to the right zygomatic region. The mass showed objective regression when 3,000 rads in 3 weeks had been delivered using orthovoltage (factors as described previously).

During the following year she developed multiple metastases to bone, including destruction of the pedicle of the eleventh thoracic vertebra. Soft tissue lesions in lung and cul de sac also occurred.

The combination of local radiation therapy at doses of 1,000 rads to 2,000 rads over a period of 1 to 2 weeks, and chemotherapy, resulted in rapid regression of measurable lesions and relief of symptoms.

In October, 1965, she developed pain in the buttocks and became incontinent of urine and

feces. These symptoms occurred over a 48 hour period. Radiation therapy was directed to the spinal cord from the level of T-12 to L-5. Initial dose fraction was 25 rads and daily doses were increased gradually thereafter until a final dose of 2,975 rads in 21 elapsed days had been delivered. Corticosteroids were not administered concomitantly. Within 2 weeks her signs and symptoms had regressed completely; the start of this regression was noted within the first 3 days.

She remained relatively well for the next several months, receiving palliative local irradiation and chemotherapy to various sites of metastases. Symptomatic improvement and objective regression of lesions occurred on each occasion.

In July, 1966, she developed sudden severe back pain, motor weakness of both lower extremities, urine and fecal incontinence; all symptoms were of 24 hours' duration. On physical examination, 3+ to 4+ hyper-reflexia was noted in lower extremities but sensation to pinprick was intact. Roentgenography revealed osteolytic destruction of the third, sixth, eleventh and twelfth thoracic vertebral bodies due to metastases.

Myelography from the lumbar space was not successful and was considered to indicate a block. Contrast material injected into the cisterna magna failed to pass the level of C-7 to T-1.

Two milligrams of Decadron was administered intravenously (and continued every 6 hours thereafter) and irradiation at high initial dose rate was begun. A dose of 750 rads, using orthovoltage (factors as described previously), was delivered to the spine from C-6 to T-10 on the first day, and this was repeated on the second day. Thereafter, dose rates of 200 rads per day were delivered for a total dose of 2,900 rads in 10 elapsed days.

Within 24 hours of the first treatment, she exhibited no further deterioration. Within 72 hours, she had experienced relief of pain. At the end of 1 week she had regained voluntary movement of her lower extremities and control of bowel and bladder functions.

Over the next month she exhibited a progressive downhill course and died of disseminated disease.

Case IV. P. F., a 6 8/12 year old girl, was seen first at Children's Hospital Medical Center in August, 1962, with symptoms of polydipsia and polyuria of 4 months' duration. Enuresis, weight gain and diminished appetite were present also. No other symptoms were noted and physical examination was entirely within the limits of normal.

After exhaustive evaluation, she was diagnosed as having mild diabetes insipidus of an organic nature.

She remained relatively well until January, 1967, when she developed poor vision which progressed over a 2 month period. Occasional generalized headache and apathy were associated symptoms.

Physical examination now revealed poor essential vision and bizarre peripheral fields. At pneumoencephalography, a soft tissue lesion in the region of the anterior third ventricle was outlined and some deformity to the shape of the super pineal recess was observed. The lateral ventricles were dilated moderately.

She underwent craniotomy and a tumor was removed from the hypothalamus and optic pathways. Microscopic examination revealed a lesion consistent with undifferentiated "atypical" pinealoma. Radiation therapy was directed to the entire skull and consisted of 3,550 rads using orthovoltage (technique as described previously) in 17 elapsed days. A total higher dose of 4,550 rads in 26 elapsed days was delivered to the site of the primary lesion in the anterior fossa.

She remained well until January, 1968, when she developed recurrent and progressive low back pain which did not radiate. Physical examination was not remarkable.

In early February, however, she suddenly was unable to void and motor power of the lower extremities became diminished. Physical examination revealed hypoesthesia below T-6 and there were hyperactive and symmetric deep tendon reflexes of the lower extremities. Seven hundred milliliters of urine was obtained upon catheterization of the bladder. The remainder of the physical examination was negative. Roentgenography of the spine revealed no abnormality.

Myelography at the interspace between L-3 and L-4 revealed thick yellow fluid. Five milliliters of pantopaque was instilled into the subarachnoid space and an irregular column of the contrast material was noted with a block to the free flow of the dye column at L-2 (Fig. 1, *A* and *B*), an additional 1 ml. of contrast medium

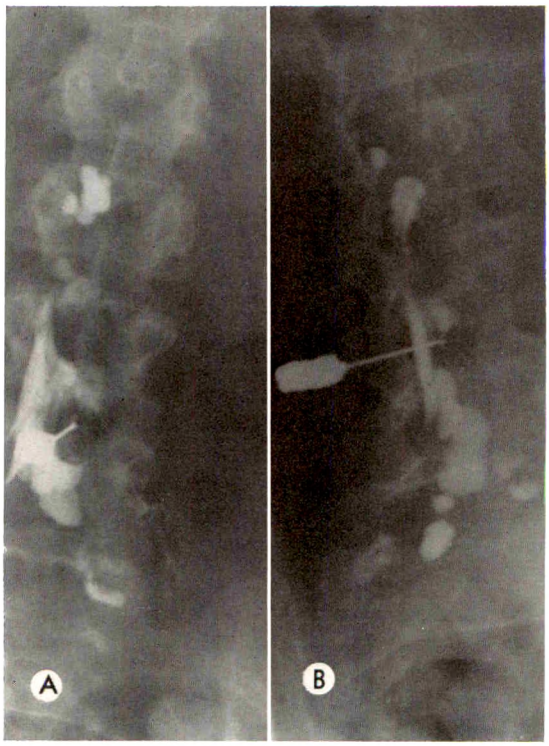


FIG. 1. Case IV. (*A*) Posterior and (*B*) lateral myelograms. Contrast medium injected into the lumbar spine at the interspace between L-3 and L-4 shows concave deformities due to metastases. There is a block at L-2.

was instilled into the cisterna magna and a block to the free flow distally was noted at the level of T-5 (Fig., 2, *A* and *B*).

Six milligrams of Decadron was administered intramuscularly (to be followed by 2 mg. by mouth every 6 hours) and radiation therapy consisting of 750 rads, using orthovoltage (factors as described previously), was delivered from the level of T-5 to S-1. Within 12 hours, her sensory level had increased to T-4. Because of the diffuse area involved, emergency laminectomy was withheld and an additional 750 rads was delivered to the same volume 24 hours after the initial treatment. In addition, 300 rads now was delivered to the spinal cord from the level of C-1 to T-4.

By the afternoon of the second day of irradiation (approximately 30 hours after radiation therapy began) her neurologic state improved in that her sensory level reverted to T-6, as on admission.

Within 48 hours of the start of radiation therapy her sensory level disappeared and sensation was normal, reflexes became 1+ and symmetrical throughout; she was able to walk unassisted and she voided spontaneously.

On the third day of treatment, daily fractions of radiation were reduced to 150 rads and a total dose of 2,500 rads to the spinal cord was delivered in 15 elapsed days. A myelogram, performed with the retained contrast material in the subarachnoid space at 1 week from the start of therapy, showed free flow of contrast medium with resolution of the blocks.

CASE V. S. W., a 3 9/12 year old boy, was well until August, 1966, when he fell, developed pain in the left leg and was unable to support his weight.

By October, 1966, a mass had appeared in the left inguinal region. Roentgenology revealed osteolytic destruction of the iliac bones and of all of the thoracic and vertebral bodies. The ninth thoracic vertebral body was totally collapsed. A large soft tissue mass with amorphous calcification was present in the right suprarenal area.

Biopsy of the inguinal lymph node confirmed the diagnosisis of neuroblastoma and chemotherapy was begun.

Within several days of admission he had developed analgesia in the distribution of S-1 to S-4 involving the buttock and lateral aspect

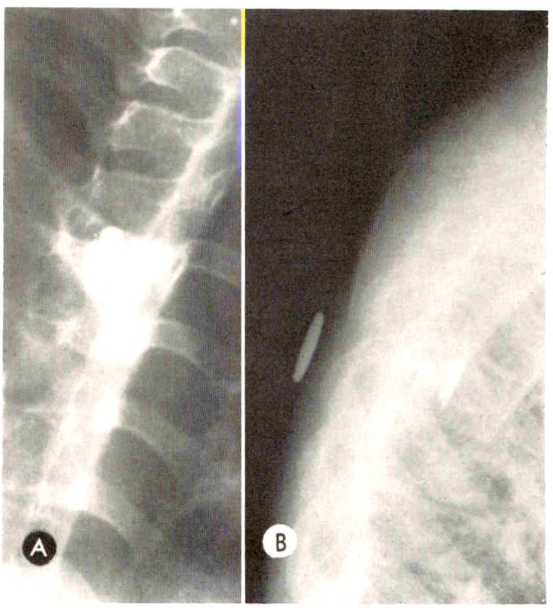


FIG. 2. Case IV. (*A*) Posterior and (*B*) lateral projections demonstrate contrast medium injected into cisterna magna blocked at T-5.

of the foot on the right side. Absent deep tendon reflexes were noted in the lower extremities and a left Babinski sign was present.

Radiation therapy was administered through a portal which encompassed the spine from the level of T-6 to L-5, the right suprarenal area, and the sacrum, in continuity. A dose of 1,480 rads in 9 elapsed days, using orthovoltage (factors as described previously) was delivered at a daily dose rate of 150 rads. He experienced no untoward symptoms and his neurologic signs regressed gradually over the next 2 weeks.

He remained relatively well until December, 1966, when he developed symptoms of cord compression: incontinence of urine and feces and paraplegia became manifest over a 3 day period; a sensory level was present at the T-3 to T-5 region; absent deep tendon reflexes were noted in lower extremities and a positive Babinski sign was apparent on the left.

Because he was considered too ill for myelography, irradiation was delivered without roentgenographic documentation of the clinically determined level of spinal cord involvement. A dose of 750 rads, using orthovoltage (factors as described previously), was delivered from the level of T-2 to T-6 spinal cord on 2 consecutive days each, 500 rads on the third day, for a total dose of 2,000 rads in 5 elapsed days.

At 48 hours from the start of radiation therapy he exhibited voluntary movement of his right foot. At 96 hours he had regained sensation to pin prick in his lower extremities. Within 6 days from the start of radiation therapy he could void spontaneously and had bowel control.

He remained relatively well for several weeks but then exhibited increasing widespread metastases and died shortly thereafter.

Case vi. D. C., a 17 year old boy, experienced mild left knee pain and swelling of his lower left thigh in July, 1963. Biopsy of a destructive lesion of the distal left femur was interpreted as neuroblastoma. Intensive evaluation for a primary lesion, including exploratory laparotomy, failed to reveal any other abnormality.

He was treated by radiation therapy (6,000 rads in 6 weeks; 2 mev. Van de Graaf), and chemotherapy. The symptoms improved and the mass regressed.

In January, 1965, he developed a metastatic focus in the left lower lung field which was excised.

In April, 1965, he was referred to Children's Hospital Medical Center. At this time he had developed an osteolytic lesion due to metastasis in both the left humerus and left parietal bone of the skull and he had a recurrent nodule in the left lower peripheral lung field.

Following admission he was treated with palliative radiation therapy (2,000 rads in 2 weeks, orthovoltage factors as described previously) to the involved areas and chemotherapy was re-instituted. Symptoms of pain in the areas of bone metastases vanished and objective regression of the nodule in the left lower lung field was documented by roentgenograms of the chest.

He remained well until July, 1965, when he developed acute back pain. Physical examination revealed 3+ deep tendon reflexes of both lower extremities, limitation to straight leg raising and tenderness over the ninth thoracic vertebra. Sensory examination was negative. Roentgenograms of the spine showed no evidence of obvious abnormality.

Radiation therapy was directed to the lumbar spine from the level of L-1 to L-5; 400 rads per day was administered to a total dose of 2,000 rads in 6 elapsed days, using orthovoltage (factors as described previously).

Marked relief of pain occurred within this treatment course and his signs diminished.

In August, 1965, he returned because of a 3 day history of recurrent back pain which radiated to each inguinal area, weakness of both lower extremities and inability to urinate.

Roentgenograms of the spine were negative.

Neurologic examination revealed bilateral positive Babinski signs, absent deep tendon reflexes in the left lower extremity and 3+ in the right lower extremity. He was unable to stand and he could not hold his legs upright while he was in the supine position. Sustained clonus in the right leg was noted. Sensation was intact.

A myelogram revealed a complete block to the free flow of contrast medium at the interspace between T-11 and T-12. The cerebrospinal fluid protein content was 67 mg. per cent.

Radiation therapy was instituted immediately; 1,000 rads, using orthovoltage (factors as described previously), was delivered to the spine from the level of T-9 to T-12. On the second day, an additional 500 rads was delivered (Table II). In conjunction, 5 mg. of Decadron was administered intramuscularly and was followed by 4 mg. by mouth at 5 hour intervals.

Within 6 hours of the first treatment, sensation to pain had diminished over the anterior aspect of the right thigh. However, by 24 hours from the first treatment, sensation had returned to normal throughout and his back pain was not apparent. Within 72 hours he was able to move both lower extremities voluntarily. At 5 days he was able to void spontaneously; a repeat myelogram at this time showed complete resolution of the block.

DISCUSSION

Previous reports have discussed the role of radiation therapy for extradural metastases in lymphoma[1,4,7] and in a limited number of patients with carcinoma.[4] There is agreement that the problem is an emergency one and that the consequences of spinal cord compression should be avoided regardless of how advanced the disease might be. General agreement also exists that the success of irradiation is greater if the symptoms of spinal cord involvement are of relatively short duration, and that surgical decompression should be performed if symptoms and signs are rapidly progressive over a 24 hour period.

Uniformity of opinion does not exist, however, regarding initial fractions of irradiation, although one report has noted no difference in response between patients treated with equal doses of irradiation and those treated with low initial dose. Except in one patient, high initial dose has not been evaluated.[4]

Although there may be benefit from chemical therapy prior to beginning radiation therapy,[7] this is indefinite[4] and no evaluation of therapy with corticosteroids has been reported in this clinical situation.

In the years prior to 1963, our policy of treatment included initial daily doses of 25 rads to the area of involvement as outlined by clinical signs, symptoms and roentgenographic evaluation. If deterioration of the clinical condition occurred within the ensuing 12 to 24 hours, then immediate surgical decompression would be undertaken and irradiation would be administered postoperatively in standard daily fractions of 150 to 200 rads for tumor control. If the patient's condition was stable, however, the initial dose fraction would be doubled on each successive day until a daily fraction of 150 to 200 rads was attained. The final dose would be consistent with palliative treatment to control the particular neoplasm. Surgical decompression was undertaken as the first treatment modality if the neoplasm was known to be unresponsive to moderate doses of irradiation.

In patients with widely separated lesions involving the spinal canal, those with vertebral body involvement or those whose clinical condition implied that a surgical procedure might carry a high morbidity or mortality rate, a surgical decompression seemed best avoided if possible. A radiotherapeutic approach to minimize the need for surgical intervention seemed preferable.

It had been our impression from previous experience that low initial dose irradiation in this clinical situation carried a similar risk of continued tumor growth and worsening of the clinical picture, as that reported when initial low doses are administered for a different but not dissimilar problem.[3,8] Therefore, we decided on a policy of high initial dose irradiation for spinal cord compression due to metastases and, hopefully, thus to eliminate, or at least minimize, the need to subject the patient to surgery in order to accomplish the same immediate goal; *i.e.*, relief of impending spinal cord transection.

Despite previous work,[3] we decided to combine radiation therapy with the administration of corticosteroids to diminish any possible edema induced by irradiation in these critically compromised volumes. This policy follows that outlined in another critical situation in childhood neoplasia,[2] as described for intracranial pathology generally,[6] and as will be discussed in a future publication separately by one of us (A.M.). Our present recommendation is the oral or intravenous administration of Dexamethasone at a dose of 0.2 mg. per kg. body weight, given in 4 equal doses at 6 hour intervals.

We would like to emphasize the need to

evaluate carefully the neurologic status of each patient in this treatment protocol. Prior to and following the initial dose of irradiation, careful neurologic evaluation is performed at 1 hour intervals to detect any worsening in clinical status which might require surgical intervention.

SUMMARY

This report is too limited to evaluate the full efficacy of this approach to spinal cord compression. However, certain points might be emphasized: (1) Each patient in this small series had a neoplasm that had been demonstrated previously to be sensitive to the effects of irradiation; (2) no patient in this limited report exhibited a significant worsening of his clinical condition and required a decompression laminectomy; and (3) symptoms of moderately advanced spinal cord compression, as noted by a sensory loss and sphincter control loss, were reversible and function was regained.

It is our hope that by demonstrating the efficacy of this approach in these few patients,* larger numbers of patients might be evaluated in greater detail, and that both the incidence of reversal of spinal cord compression by radiation therapy might be increased and the need for surgical decompression diminished in patients whose lesions are radioresponsive.

* Within the past few months we have treated 2 additional patients with the diagnosis of Ewing's sarcoma who have developed metastatic disease to the spinal column. Both patients developed signs and symptoms of impending spinal cord compression and each was treated with high rapid dose irradiation. Both patients demonstrated resolution of their neurologic deficit within 24 to 28 hours of the initiation of treatment. In each case, corticosteroid therapy was combined with radiation therapy.

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THE ARTERIOGRAPHIC EVALUATION OF MILITARY VASCULAR TRAUMA*

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THE rapid evacuation program along with the primary repair of arterial injuries has resulted in a high percentage of lives saved and a low amputation rate in the Vietnam conflict.[7,11,12,18] This has resulted from a combination of advanced medical-surgical techniques in concert with advanced communication and transportation developments.[11] Hence, it becomes the physician's responsibility to provide the returning wounded with the best follow-up care possible in both military and civilian practice.[7,15] It is the purpose of this communication to emphasize one aspect of this care. Arteriography has received some attention in the evaluation of civilian trauma;[4,6,8,10,14,16,20] however, there has been little emphasis on the use of angiography in the evaluation of sequelae to military trauma.

One must be aware of the possible vascular complications of military wounds; the most accurate delineation of arterial complications is with the application of angiography. This report deals primarily with the complicating sequelae to arterial injuries in the extremities, but the same principles might apply to wounds anywhere in the body. The time sequence in the development of a vascular complication may be variable. Some complications become evident within days to weeks following the injury, whereas others may take months or even years before they reach a magnitude of overt manifestation.

DISCUSSION

Fundamentally the various types of military vascular wounds and complications are similar to civilian injuries, with the important exceptions of more massive trauma to tissues, comminuted fractures, increased frequency of multiple injuries,[7] large amounts of metallic foreign body fragments, and the necessarily greater speed of treatment to save life and limb. In addition the pressure of combat and multiple wounded must also be considered.[9] Fractures, muscular damage, neurologic or vascular injury will all influence the type of surgery and treatment.[1] It is the peripheral vascular complication that concerns this report.

Arteries may be penetrated, lacerated, occluded by edema,[4] thrombosed,[1] and damaged by bone fragments initially or after manipulation.[1,6] Against the pressure of multiple wounded and combat the surgical repair cannot be perfect in every case; many lesser arterial injuries may be overlooked.[2,6,7] The vascular bed in being dynamic, pulsatile, affected by local factors or repeated injuries, has strong propensity to change. Therefore, with time and the influence of minor trauma or retained foreign body metallic fragments, small and overlooked lesser injuries may amplify to a recognized complication. The *physician-angiographer* should have an awareness of the major areas of complication when evaluating previously traumatized areas. He should also be aware of the pitfalls in the clinical evaluation of these vascular complications.

ARTERIAL OCCLUSION

Modern treatment of arterial injuries does not allow ligation as a procedure of first choice. Primary anastomosis with restoration of vascular continuity has been

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This material has been reviewed by the office of The Surgeon General, Department of the Army, and there is no objection to its presentation and/or publication. This review does not imply any indorsement of the opinions advanced or any recommendation of such products as may be named.
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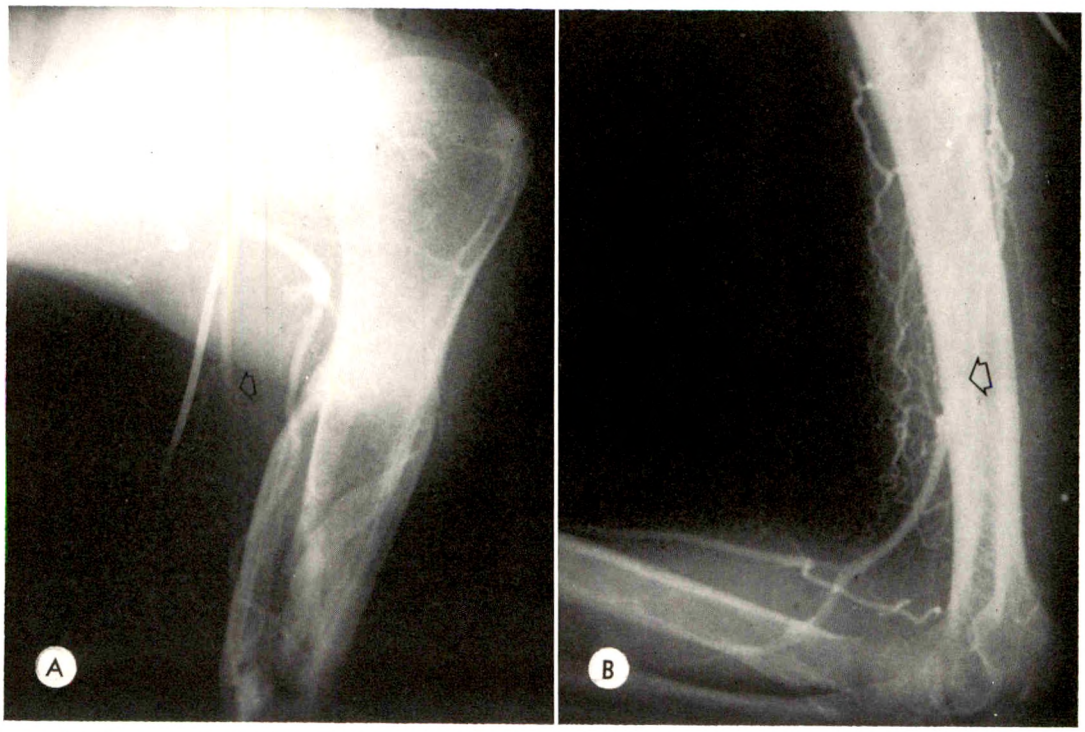


Fig. 1. (*A*) Lacerated brachial artery requiring ligation (arrow). (*B*) Collateral development over a period of 6 months establishes reconstitution of brachial artery (arrow) with normal distal tributaries.

proven to save more extremities,[12] and is now accepted as the proper method of treatment in both military and civilian arterial wounds.[2,5] The emergency treatment of arterial injuries is now compression dressing or pack. Tourniquets are no longer permitted if there is anticipation of primary arterial repair, as they can produce further injury to soft tissue or vasculature and may make amputation necessary.[1,2] Compression bandage or pack better preserves the remaining viable tissues and minimizes further injury to the vital arteries. This provides for salvage of the arterial tree and the viability of the extremity. Also, the diagnosis of arterial spasm must be held suspect.[9,19] While arterial spasm is a true entity, its presumed presence may unnecessarily delay the exploration of the artery and its possible repair.[5,9] Cases of true occlusion or laceration will be discovered more rapidly if the diagnosis of arterial spasm is avoided.[3,6] Furthermore, distal pulses may be present despite arterial laceration.[2]

Arterial continuity can be accomplished by direct suture, anastomosis, interpolation of grafts, or relief of surrounding pressure. If arterial ligation or occlusion cannot be avoided, the best chance for collateral arterial development occurs in the upper extremity.[1] Angiography at future dates may be indicated to follow the progression of this collateralization in the interest of evaluating the need for measures to preserve the viability and usefulness of the extremity[13] (Fig. 1, *A* and *B*).

Arteriovenous Fistula

Arteriography in the evaluation of a possible arteriovenous fistula is indispensable. The arteriovenous fistula may develop over a period of time in an area of injured vasculature or as a surgical sequela.[2] The peripheral pulses may be normal and the continuous murmur of an arteriovenous fistula may be confused with the systolic bruit of a pseudoaneurysm.[14] The arteriovenous fistula may also simulate an abscess. In areas of overlooked relatively minor arterial wall

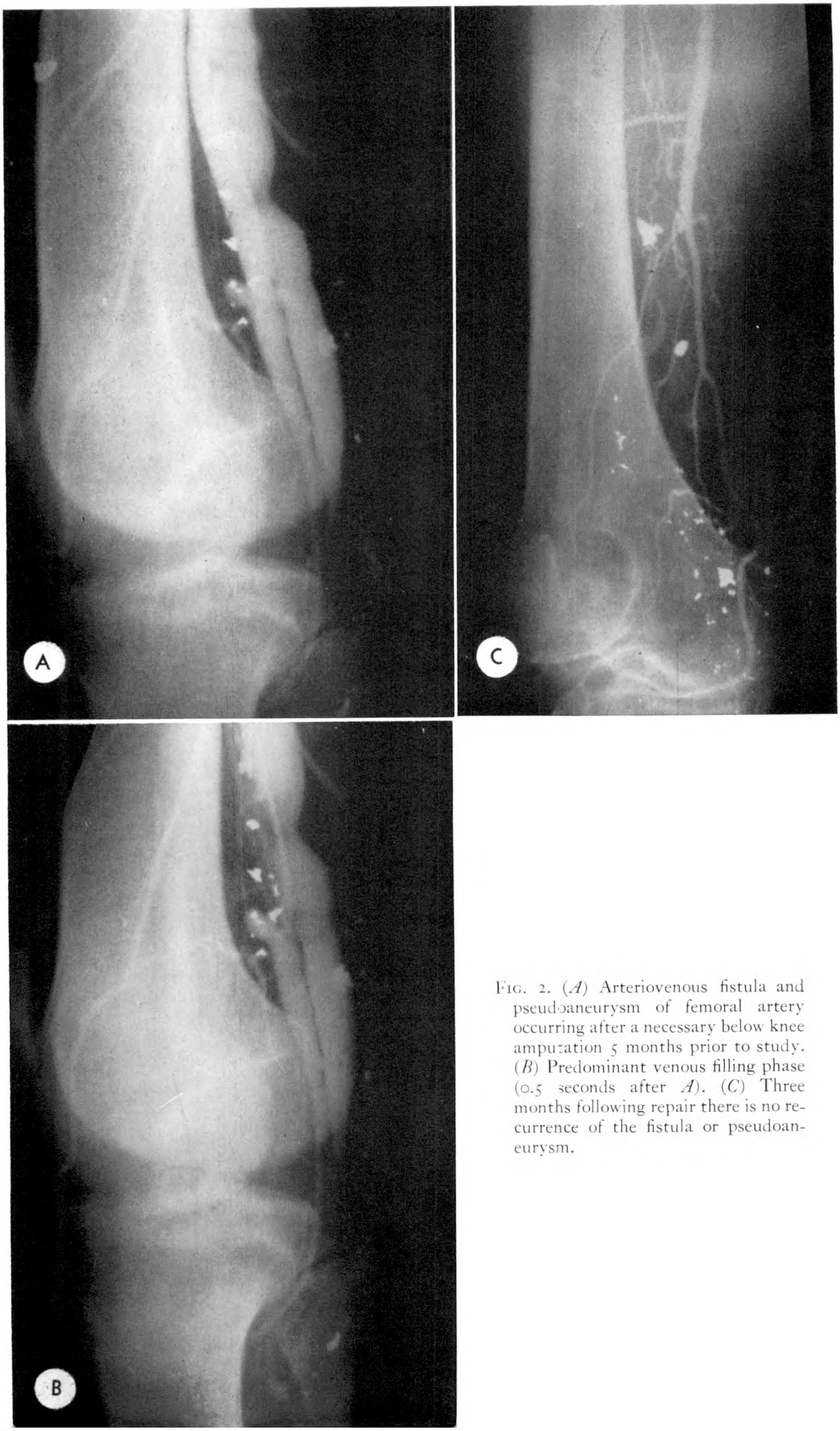


FIG. 2. (*A*) Arteriovenous fistula and pseudoaneurysm of femoral artery occurring after a necessary below knee amputation 5 months prior to study. (*B*) Predominant venous filling phase (0.5 seconds after *A*). (*C*) Three months following repair there is no recurrence of the fistula or pseudoaneurysm.

injury, constant pulsatile pressures, foreign body fragments, and postinfection alterations, an arteriovenous fistula or pseudoaneurysm may develop as a late complication. Arteriography can easily demonstrate the site, size, extent, and associated injury at the fistula site (Fig. 2, *A-C*; 3; and 4, *A* and *B*). The postoperative repair of the fistula may also be evaluated (Fig. 2*C*).

In the author's experience with military wounds, the arteriovenous fistula is often associated with the formation of a pseudoaneurysm (Fig. 2, *A–C*; 3; and 4, *A* and *B*). This is a logical occurrence since sufficient injury to create an arteriovenous fistula must also cause injury to adjacent areas of the arterial wall; thus allowing for the development of a pseudoaneurysm.

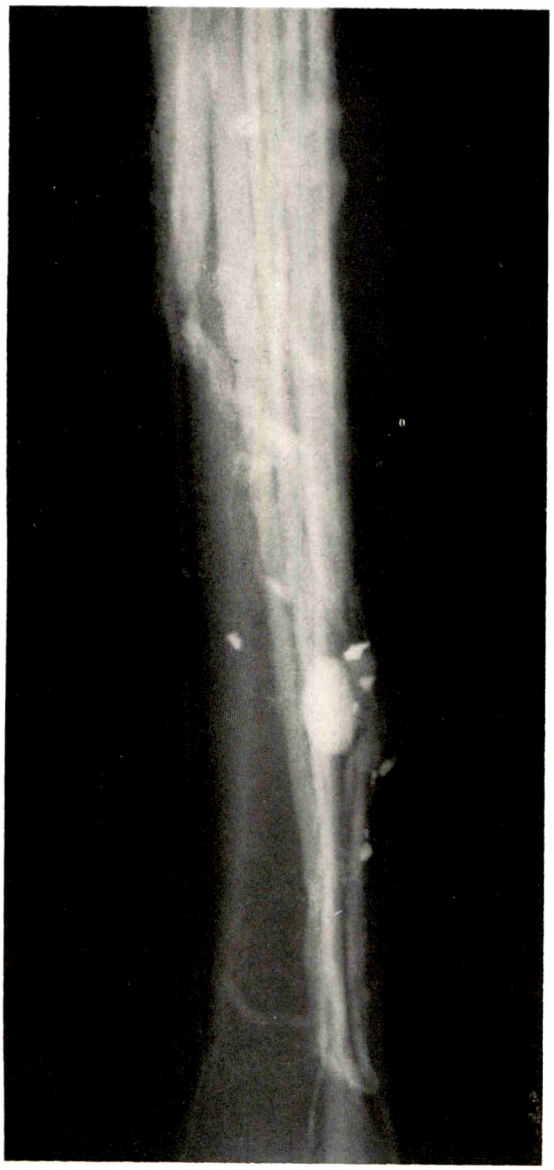


Fig. 3. Pseudoaneurysm and arteriovenous fistula demonstrated 7 weeks following leg injury.

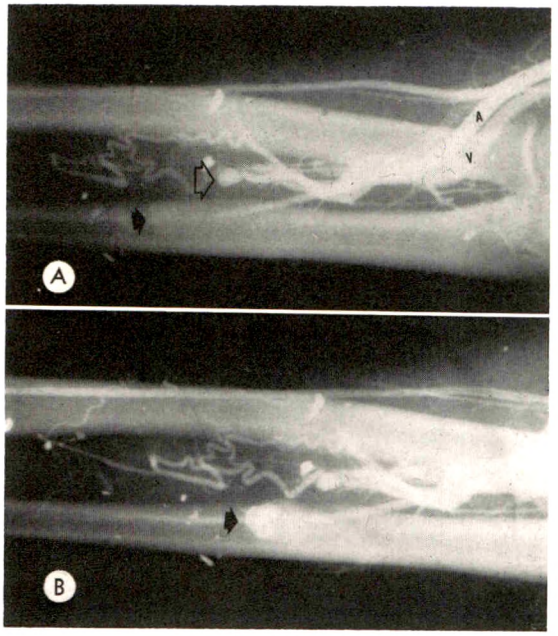


Fig. 4. (*A*) Arteriovenous fistula with brachial artery (A) and early brachial vein (V) filling from posterior interosseous arteriovenous communication with an associated pseudoaneurysm (open arrow) studied 8 months following injury. (*B*) A larger pseudoaneurysm of the ulnar artery is also present (black arrow). The radial artery is intact and uninjured.

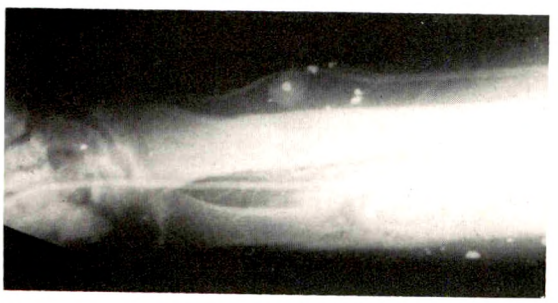


Fig. 5. Pseudoaneurysm of distal radial artery discovered 1 year after injury. Small filling defects represent thrombus within the pseudoaneurysm. Note also the association of the metallic fragment with the area of injury.



Fig. 6. (*A*) Large pseudoaneurysm of proximal forearm with vascular displacement. Injury occurred 6 months prior to arteriography. (*B*) Peripheral blush (arrows) of pseudoaneurysm due to internal thrombus.

PSEUDOANEURYSM

The pseudoaneurysm or "false" aneurysm is a hematoma in direct continuity with the arterial lumen. It does not have the media and adventitia of a true aneurysm but only the intima which forms after the aneurysm has persisted for a long period of time.[14] It can achieve considerable size and may also simulate an abscess since it may not be pulsatile.[1,14] The true size of the pseudoaneurysm is not always demonstrable by angiography, since it can be filled with varying amounts of thrombus. Spontaneous thrombosis of the pseudoaneurysm, an unusual occurrence,[15] may also occur (Fig. 7). Filling defects in the pseudoaneurysm are caused by thrombus (Fig. 5). The true size of the pseudoaneurysm may be estimated by palpation and/or displacement of vessels demonstrated on the arteriogram (Fig. 6*A*). The sac may be completely filled with thrombus except for a peripheral blush (Fig. 6*B*). As mentioned previously, the pseudoaneurysm may be associated with an arteriovenous fistula (Fig. 3; and 4, *A* and *B*). The peripheral pulses may be normal as they may also be with the arteriovenous fistula.[14] Therefore, the late sequela of the pseudoaneurysm should be considered and evaluated angiographically when indicated.

SUMMARY

The rapid evacuation of military wounded and the emphasis on restoration of vascular continuity rather than arterial ligation has been proven to save more lives and extremities than ever before in American military history. However, the proper follow-up care and evaluation of these re-



Fig. 7. A 20 year old soldier received fragment injuries to his hand 3 months prior to study and had a residual pulsatile mass. However, the pulsatile mass disappeared 1 week prior to the arteriography. The irregular artery demonstrated (arrow) probably represents residual of now thrombosed pseudoaneurysm.

turning wounded require an appreciation of the types of military injuries as well as the possible sequelae and complications. Angiography is indispensable in the elucidation of such complications as arteriovenous fistula, pseudoaneurysm, and in the evaluation of collateral arterial development. In this way angiography keeps pace with the improved surgical techniques to the ultimate benefit of viable useful extremities.

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ARTERIOGRAPHY OF THE EXTREMITIES*

WITH AN ANALYSIS OF THE OCCLUSIVE DISEASES OF THE ARTERIES IN THE LOWER EXTREMITIES

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IT IS the consensus that the enormous advances in angiography in recent years are the most brilliant in the field of diagnostic radiology. The improvement in contrast agents[10] and the development of seriographic apparatus and x-ray television systems have undoubtedly played an important role in the progress of angiography. At the same time, the accomplishments made by pioneers such as Moniz[12] in cerebral angiography, dos Santos and associates[4] in aortography, Forssmann[7] in cardiac catheterization, and Seldinger[14] and his Swedish colleagues in the percutaneous catheterization of arteries, as well as the selective arteriography of the viscera, should never be forgotten in the history of angiography.

The first roentgenographic demonstration of the peripheral vessels of the living human was performed by Berberich and Hirsch in 1923:[1] they visualized the peripheral vessels by an injection of strontium bromide solution. In the following year, Brooks[2] demonstrated the femoral artery at the proximal end of the Hunter's canal and injected sodium iodide solution into the artery under general anesthesia for visualization of the arterial system of the lower extremity.

Despite the rapid progress in angiography of the brain, viscera of the trunk, heart and the great vessels, angiography of the extremities has always been "a neglected stepchild," probably because instrumental development has bestowed little benefit on the latter.

Unlike the era of Brooks, the surgical reconstruction of the diseased artery is now not uncommon in surgical practice. The accurate visualization of the pathologic processes in the artery and the complete understanding of the circulatory disturbances in the involved limb may be indispensable for the operative intervention on the diseased artery. For example, the visualization of a segmental occlusion in the femoral or popliteal artery is not always sufficient to explain the whole clinical picture of a patient with intermittent claudication and/or a gangrenous foot, since some of those pictures may well be caused by additional, more distally located occlusion or occlusions in the arterial system of the lower extremity (Fig. 1; and 2, *A* and *B*). In such a case the operative intervention on the segmental



FIG. 1. Right femoral arteriogram in a 51 year old man with gangrenous toes (age at onset: 39 years). There is occlusion at the lower end of the femoral artery.

* From the Department of Radiology, the Tokyo Medical and Dental University School of Medicine, Tokyo, Japan.

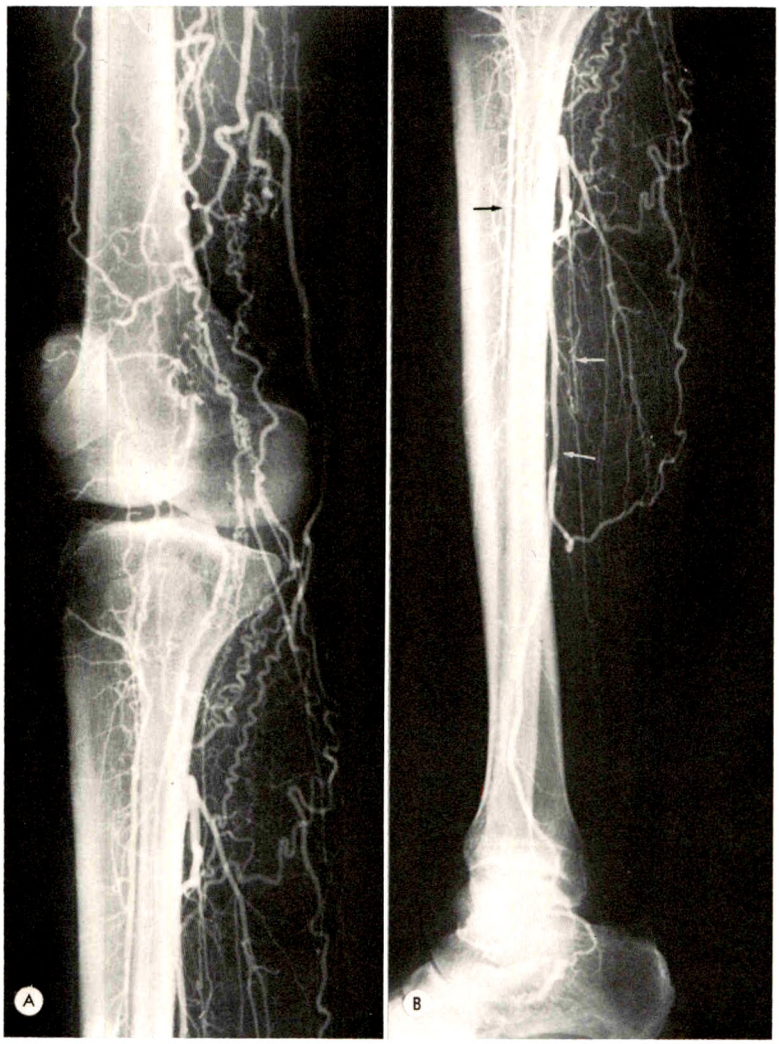


Fig. 2. Same patient as in Figure 1. (*A*) A number of tortuous collateral arteries in the knee region are shown. (*B*) The proximal portion of the anterior tibial artery (left arrow), posterior tibial artery (2 right upper arrows) and peroneal artery (right lower arrow) are revisualized.

occlusion in the proximal portion alone may not be effective.

It is the author's opinion that the complete visualization of the arterial system of the limb, preferably on a long noninterrupted roentgen-ray film may be a prerequisite to the preoperative evaluation of the arterial pathology in the extremity. An arteriogram of the whole limb on the long roentgen-ray film is definitely more convenient to the radiologist than an arteriogram of the whole extremity on 3 cut films laid end-to-end (Fig. 3; 4, *A* and *B*; and 5).

Figure 3, a femoral arteriogram in a 54 year old man with intermittent claudication in his left leg and gangrene in the little finger of his hand, reveals a sandglass-like stenosis in the popliteal artery. Figure 4, *A* and *B*, a femoral arteriogram in a 53 year old man with intermittent claudication in his left leg, discloses a segmental occlusion in the popliteal artery. It is unquestionable that the former arteriogram, on which a junction of the cut films happens to coincide at the uppermost portion of the arterial stenosis, is inferior in quality to the latter from the roentgenographic as well as diagnostic points of view. Figure 5

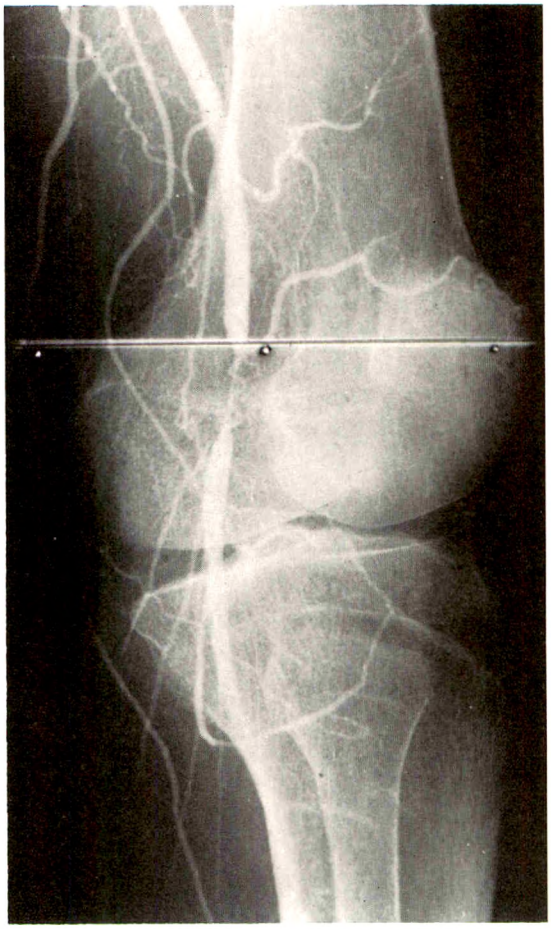


Fig. 3. Segmental stenosis in popliteal artery.

is an arteriogram of a patient with a traumatic arteriovenous fistula between the popliteal artery and vein in the popliteal fossa. Although the junction of the cut films has no influence upon the result of diagnosis, such discontinuity on the roentgenographic image should be avoided, if possible.

When the author became interested in angiography of the extremities at the Tokyo Medical and Dental University Hospital 4 years ago, he decided to use a long cassette containing a 25×90 cm. roentgen-ray film onto which the whole

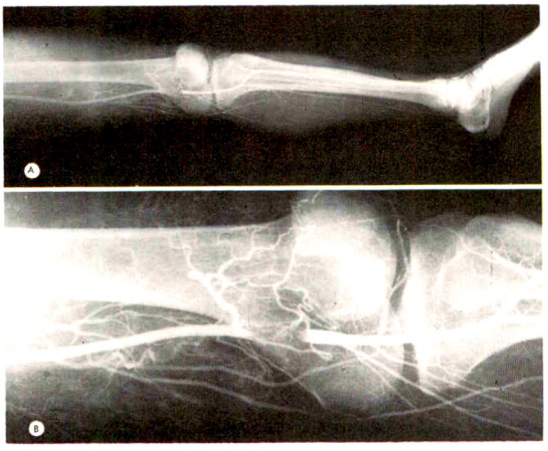


Fig. 4. (*A* and *B*) Segmental nonfilling in the popliteal artery.

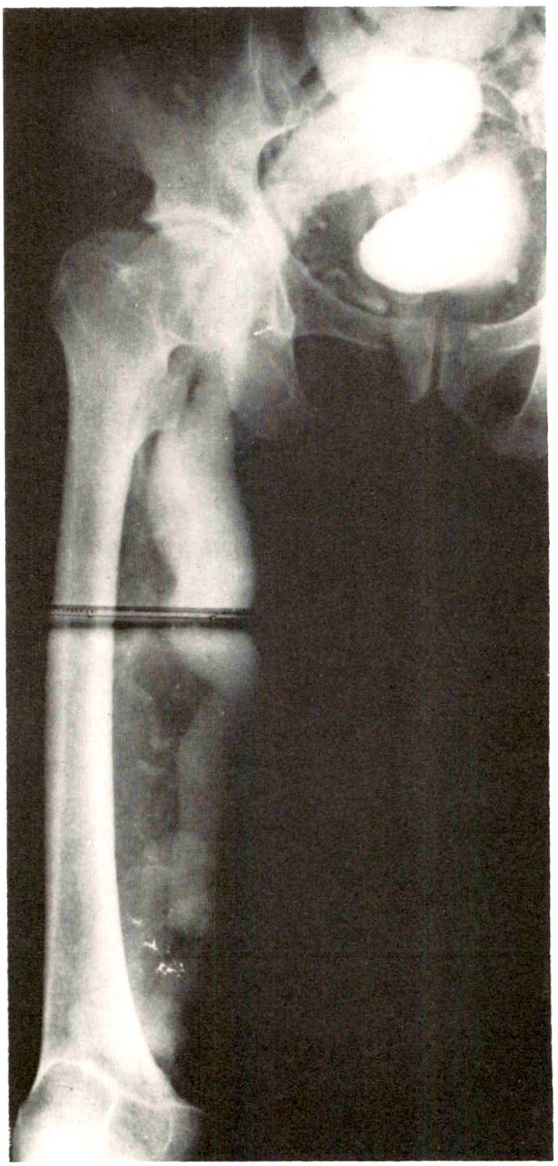


Fig. 5. Traumatic arteriovenous fistula in the popliteal fossa. The artery proximal to the fistula is enormously dilated and tortuous.

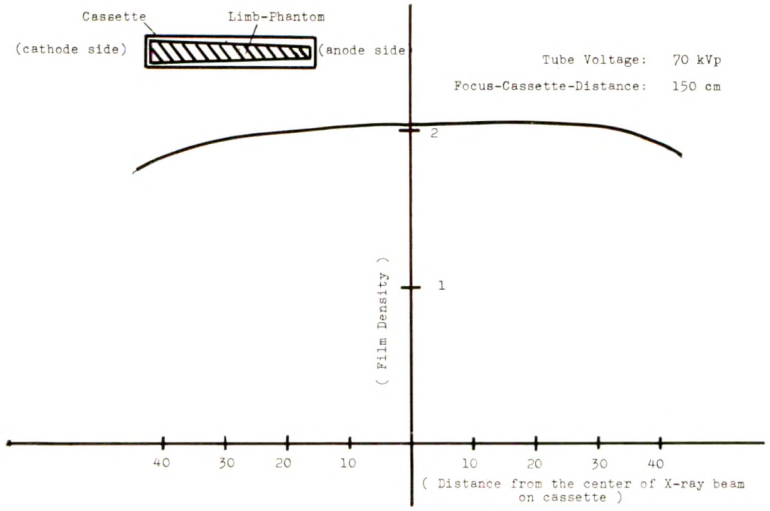


Fig. 6. Limb phantom experiment on our "differential screen."

lower limb of a Japanese could be projected. The first problem to be solved in the case of whole-limb arteriography was how to obtain a practically uniform density of diagnostic value throughout the examined extremity on an arteriogram without deterioration of the roentgenographic quality. He found that there were 2 practical methods to roentgenographically equalize the thickness or volume in the different anatomic segments of the limb: (1) A wedge-filter of thickness and shape to reflect the respective volume variations of the anatomic regions of the extremity was attached to the window of a roentgen-ray tube or inserted between the patient's extremity and the cassette; and (2) a practically uniform density in the diagnostic range throughout the examined limb was to be obtained by the use of a special screen on which intensification could reflect the respective volume variations of the anatomic regions of the limb, hereafter called the "differential screen" method (Fig. 6).

Since the author had the opportunity to employ a differential screen* for arteriography of the whole lower extremity at that time, he began to perform arteriographic examinations of the extremities, using the differential screen method instead of the wedge-filter method. From that time on, we have performed a series of 300 arteriographies of the lower extremity with excellent results over a period of 4 years.

This paper presents a description of whole-limb arteriography as performed during the 4 year period, and, in addition, the results of an analysis of a series of 106 cases of occlusive diseases of the artery in the lower extremity which were proved by arteriography.

MATERIAL

A. INSTRUMENTS

1. X-ray film: 25×90 cm. roentgen-ray film for medical use.

2. Intensifying screen: 25×90 cm. "differential screen" for whole-leg arteriography, producing neither a gap in continuity of the image of the arterial system nor discernible heterogeneity of film density (Fig. 6).

3. Cassette: The cassette must hold the roentgen-ray film and the differential screen, 25×90 cm. in size.

4. X-ray equipment: 500 ma. type diagnostic apparatus with a protecting and localizing "multi-leaf-shutter."

5. Puncturing instruments: PE No. 160 Cournand type needle with a plastic tubing of a length of 20 cm. and an inner caliber of 0.2 cm.

* Dainihon Toryo Co., Ltd. (Tokyo).

B. CONTRAST AGENTS

The following 3 contrast media were used in a majority of the cases in the present series with excellent arteriographic results:

Angio-conray (iodine content: 48.0 per cent)
Conray-400 (iodine content: 40.0 per cent)
An equal mixture of conray and angio-conray (iodine content: 38.1 per cent)

Urografin 76 per cent (iodine content: 37.0 per cent) was also used in a small number of cases at the beginning of the series but was soon given up because of its insufficient visualization of the arterial system of the lower limb.

Unlike cerebral or other visceral angiography, arteriography of the extremities is always accompanied by an excruciating pain, provoked by the injection of the contrast medium, unless the patient is placed in a deep anesthetic or analgesic status. Insofar as pain is concerned, with an equal mixture of conray and angio-conray, this is less severe than would be expected because of its lower iodine content.

C. PREPARATION AND PREMEDICATION

The patient should have nothing by mouth after midnight if the procedure is to be performed in the morning and nothing by mouth after breakfast if it is to be done in the afternoon. A small amount of the contrast medium to be used is injected intravenously to make certain that the patient will develop no untoward reaction to the contrast medium.

Sodium phenobarbital (100 mg.) and atropine sulfate (0.5 mg.) are administered intramuscularly 1 hour before the procedure, and meperidine hydrochloride (35 or 70 mg.) is given intramuscularly 1/2 hour prior to the procedure.

D. ANESTHESIA

General anesthesia by intubation or lumbar anesthesia was used in only a few patients. We were very impressed by the excellent result of the intravenous administration of FBA.1420, (Propanidid)[9] which was used in 12 patients in the present series.

A majority of the patients could tolerate the arteriographic procedure under the intravenous administration of 35 mg. meperidine hydrochloride in addition to the previously mentioned premedication, although they experienced pain or a burning sensation in the examined leg on injection of the contrast medium.

METHOD

THE LOWER EXTREMITY

The arterial needle is inserted into the femoral artery immediately below the inguinal ligament with its tip pointed upward or in the cephalic direction. The plastic tube with a stopcock, filled with 5 per cent glucose solution, is connected to the head of the arterial needle. The formation of a blood clot can be prevented by intermittent irrigation with 5 per cent glucose solution. If the patient has diabetes mellitus, a saline solution should be used rather than the glucose solution.

Fifteen cubic centimeters of conray (60 per cent solution of meglumine iothalamate) is injected in the retrograde direction with a high manual pressure, in order to obtain visualization of the external iliac as well as the common iliac arteries (Fig. 9*A*). A regular roentgen-ray film (14 ×17 inches) and an intensifying screen are used in addition to a proper antiscattering grid.

The long cassette for whole-limb arteriography is placed beneath the patient's lower extremity, and 40 cc. of highly concentrated contrast medium (angio-conray, conray-400 or an equal mixture of conray and angio-conray) is injected through the same needle during 20 seconds. Roentgen exposure is made immediately before the end of the injection of the contrast medium. The contrast material, injected in the retrograde direction from the femoral artery, usually reaches and visualizes the arcuate artery in the dorsum pedis and the arcus plantaris of the plantar artery in the foot-sole in individuals without occlusive arterial diseases of the lower extremity. The accurate time in which the contrast me-

dium may reach the arteries in the foot cannot be predicted in cases with circulatory disturbance in the lower limb secondary to arterial occlusion. Our experience in a series of 300 arteriographies of the lower extremity, however, indicates that the standard method, *i.e.*, 40 cc. of contrast medium injected for a period of 20 seconds, has made whole-leg arteriography diagnostically useful in a vast majority of the cases in this series.

The author is reluctant to insert an arterial needle into the femoral artery with its tip pointed in the distal direction, since the contrast medium injected in this manner may frequently enter the profunda femoris artery, producing excruciating pain in the back of the thigh and resulting in poor visualization of the arteries in the lower leg and foot. Furthermore, the external and the common iliac arteries cannot be examined if the tip of the arterial needle is pointed downwards or in the distal direction.

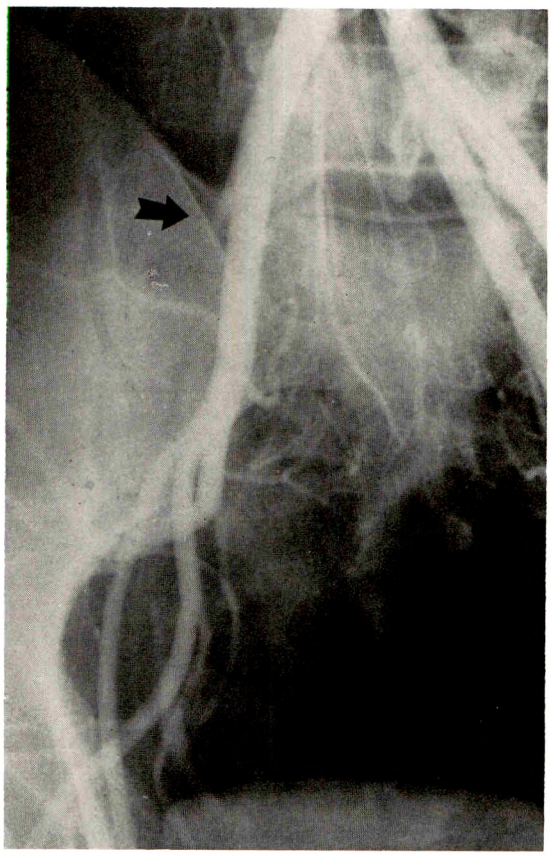


Fig. 7. Occlusion at the proximal portion of the external iliac artery (arrow) in a 35 year old man.

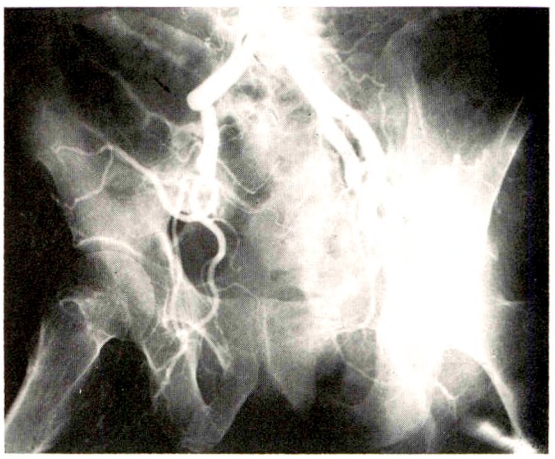


Fig. 8. Embolic occlusion in the proximal portion of the external iliac artery (arrow) developed during auricular flutter.

If the pulsation of the femoral artery to be examined cannot be palpated, a catheter is inserted via the opposite femoral artery into the lower portion of the aorta, or even into the common iliac artery at the site of examination using the Seldinger technique (Fig. 7 and 8). When the pulsation of the femoral artery cannot be palpated on both sides, either translumbar aortography or aortography by a catheter inserted into the aorta via an artery of the upper extremity is performed (Fig. 9, *A-D*).

THE UPPER EXTREMITY

The arterial needle can be inserted into either the axillary artery in the armpit or the brachial artery on the medial aspect of the brachium. In the former, one should be extremely careful not to injure the nerves around the axillary artery or to produce a hematoma at the site of the needle puncture (Fig. 10). If the brachial artery is to be used, it is not only narrower in caliber but also more easily subject to a spastic contraction on insertion of the needle than the axillary artery (Fig. 11, *A* and *B*). Twenty or 25 cc. of conray or urografin 60 per cent is sufficient to visualize the

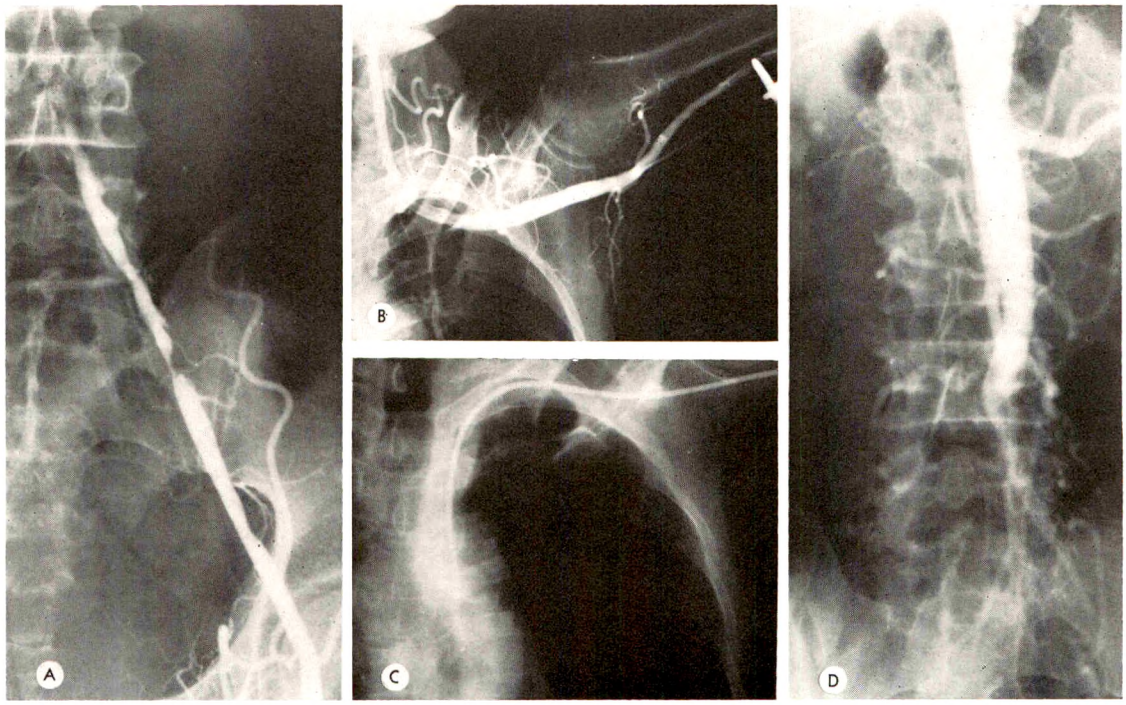


Fig. 9. Nonpalpable right femoral artery in a 75 year old man. (This case is not included in the series of 106 cases.) (*A*) Retrograde injection of the contrast medium prior to catheterization discloses stenosis in the left iliac artery. (*B*) A catheterization via the left axillary artery is attempted and the retrograde injection of the contrast material is performed prior to the catheterization. (*C*) A green catheter is advanced into the descending aorta. (*D*) The contrast material is injected through the catheter and demonstrates irregular narrowings at the lower end of the aorta and complete occlusion at the origin of the right common iliac artery.

arterial system of the whole upper extremity if the axillary artery is used.

RESULTS

During a period of 4 years, until July 31, 1968, we have performed a series of 300 arteriographies of the lower extremity by the whole-limb arteriographic technique. These arteriographies were carried out at the request of the Surgical and Medical Departments of the Tokyo Medical and Dental University Hospital. The majority of them were done by the author, although some were made by doctors under the direct supervision of the author using the previously mentioned technique.

There are 2 well-known lesions involving the arteries of the lower extremity; *i.e.*, arteriosclerosis obliterans (ASO) and thromboangiitis obliterans (TAO). The latter was originally reported by von Winiwarter as endoarteriitis obliterans in 1879 and later in 1908 by Buerger[3] as thromboangiitis obliterans. Because of Buerger's contributions to the diagnoses of the disease, it is often called Buerger's disease. Although there are a number of reports[5,6,8] in the literature which cast doubt upon the existence of a disease en-

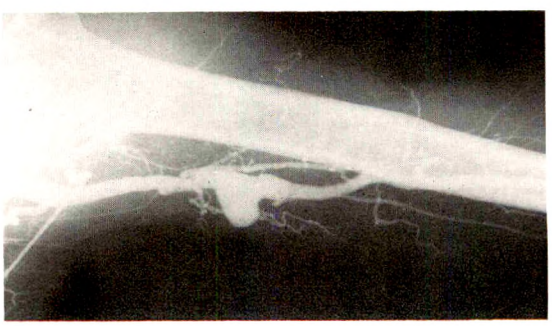


Fig. 10. Traumatic aneurysm.

tity called Buerger's disease, it is an indisputable fact that arterial occlusion in the lower limb is not infrequently encountered among Japanese of the third, fourth and fifth decades who have intermittent claudication but none of the clinical signs indicating arteriosclerosis of a pathologic degree. Since the author has so far not investigated the histopathology of the diseased artery, it is not his intention to discuss whether Buerger's disease should be considered as a specific disease entity or not.

In the present article 106 cases of occlusive arterial diseases in the lower extremity are classified into 4 types, based upon the arteriographic findings supplemented by the clinical signs (Table 1).

"Arterial occlusion of ASO type" is indicative of the cases with clinical as well as arteriographic signs of arteriosclerosis (Fig. 12, *A-C*; 13; and 21, *A* and *B*). The cases without clinical as well as arteriographic evidence of arteriosclerosis are designated as "arterial occlusion of TAO type." "Arterial occlusion of embolic type" is self-explanatory and the name is given to cases with incontroversial evidence of arterial occlusion due to embolus (Fig. 8; 27; and 28, *A* and *B*). Embolic occlusion of the artery in the lower limb developed during auricular flutter or fibrillation in 4 cases and following cardiac surgery in the remaining case in the present series. The cases not classified in the above 3 types are placed in the fourth type, that is, "arterial occlusion of unclassified type." The "unclassified type" may undoubtedly contain various diseases which cause arterial occlusion of the lower extremity. In more than one-half of the cases belonging in the "unclassified type" in the present series, however, it is believed that the asymptomatic or unnoticed TAO may become symptomatic in accordance with the progressive increase of the superimposing atherosclerotic process. The criteria upon which the differentiation between ASO and TAO is based in this article seem to be very close to the criteria of McPherson *et al.*,[11] although we place more



Fig. 11. Right axillary arteriogram in a 38 year old man with gangrene in the fingers of the right hand and the toes of both feet (clinically diagnosed as "Buerger's disease"). (*A*) Occlusion in both radial and ulnar arteries. (*B*) Spastic contraction of brachial artery is caused by the unsuccessful attempt to puncture the artery, prior to the puncture of the axillary artery.

importance on the arteriographic criteria than the clinical and exclude the history of smoking and superficial thrombophlebitis.

The average age of the 65 patients classified into the TAO type is 35.3 years at onset of the clinical signs or symptoms; the youngest patient is 21 and the oldest is 54 years. The average age at onset for the patients belonging to the ASO type is 61.0 years; the youngest patient is 35 and the oldest is 72 years. Incidentally, all patients of the ASO type in the fourth and fifth decades in the present series have a history of diabetes mellitus. It is quite interesting to note that the distribution of age at onset in a series of 101 cases of arterial occlusion of nonembolic origin indicates 2 distinct peaks separated by a deep valley (Fig. 14). Furthermore, a vast majority of the patients belonging to the younger age group have been classified into the TAO type based on the author's criteria, and a vast majority of the patients belonging to the older age group have been classified into the ASO type based upon the same criteria. The above findings can be reasonably explained by the assumption that the series may consist of 2 specific disease entities, presumably TAO and ASO, provided that diseases other than the 2 mentioned are negligible in number.

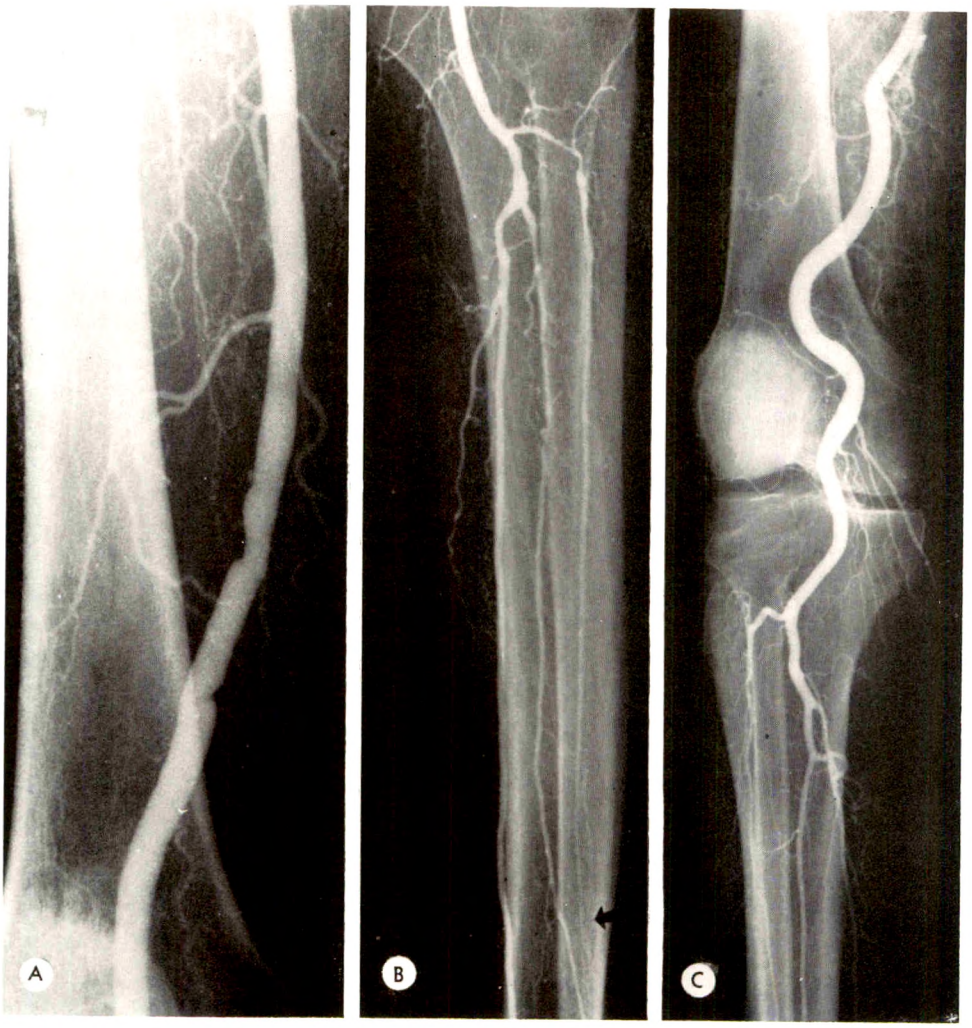
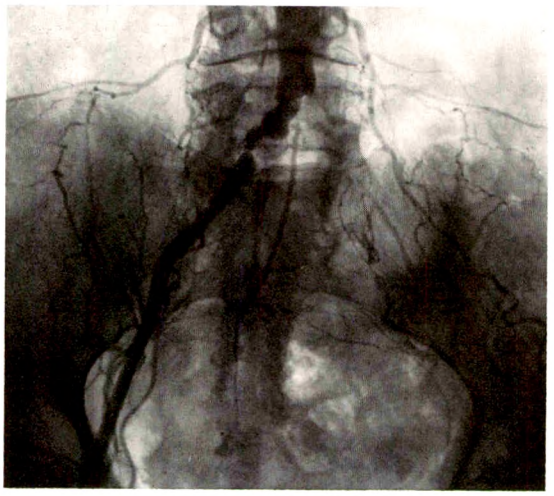


Fig. 12. (*A*, *B* and *C*) Arteriosclerotic changes appearing in the portion of the artery proximal to occlusion (arrow).



On arteriography, 4 different patterns can be distinguished at the occluded stump of the artery (at the upper end of occlusion), *e.g.*, "conical," "smoothly tapering-off," "irregularly tapering-off" and "cut-off" in shape, as schematically illustrated in Table 1. If multiple segmental occlusions are present in an artery, only the most proximal occlusion in the artery is taken

Fig. 13. Arteriosclerotic stenosis in the right common iliac artery and occlusion in the left common iliac artery in a 69 year old diabetic woman.

for an analysis of the pattern at the occluded stump of the artery. The "conical" or Pattern I (Fig. 15, *A* and *B*; and 16) and the "smoothly tapering-off" or Pattern II (Fig. 7; 17; and 18, *A* and *B*) are frequently encountered in the TAO type; on the other hand, the "irregularly tapering-off" or Pattern III (Fig. 13; and 21, *A* and *B*) is frequently encountered in the ASO type, although it is not at all infrequent in the TAO type in the late stage (Fig. 19; and 20, *A* and *B*). The "cut-off" or Pattern IV (Fig. 22; 23, *A* and *B*; and 27), which may be suggestive of an occlusion of the arterial lumen by thrombus or embolus, is frequent in the TAO type and the embolic type. It is our belief that ASO can be arteriographically distinguished from TAO or embolism in the early stage or soon after onset. The differentiation between embolism (Fig. 8; 27; and 28, *A* and *B*) and TAO (Fig. 4, *A* and *B*; 7; 11, *A* and *B*; 15, *A* and *B*; 16; 18, *A* and *B*; 22; and 23, *A* and *B*), based only on arteriographic findings in the occluded stump of the artery, may be impossible. Embolism and TAO, however, can be differentiated by the degree of development of the collateral or anastomosing routes which are absent or scanty in the former, and relatively rich in the latter, even at the onset.

Figure 24 shows the distribution of the sites of arterial occlusion in a series of 65 cases classified in the TAO type. Figure 25 demonstrates the distribution of the sites of arterial occlusion in a series of 26 cases classified in the ASO type. There is no essential difference found in the distribution of the sites of arterial occlusion in either type.

Table II indicates the incidence of gangrene in each type of occlusive arterial disease of the lower extremity. The gangrene is limited to a toe or toes in most of the cases belonging to the TAO type and the ASO type and does not extend beyond the level of the tarsometatarsal joints in any of the cases of both types. The incidence of gangrene in the involved limb is much lower in the ASO type than the

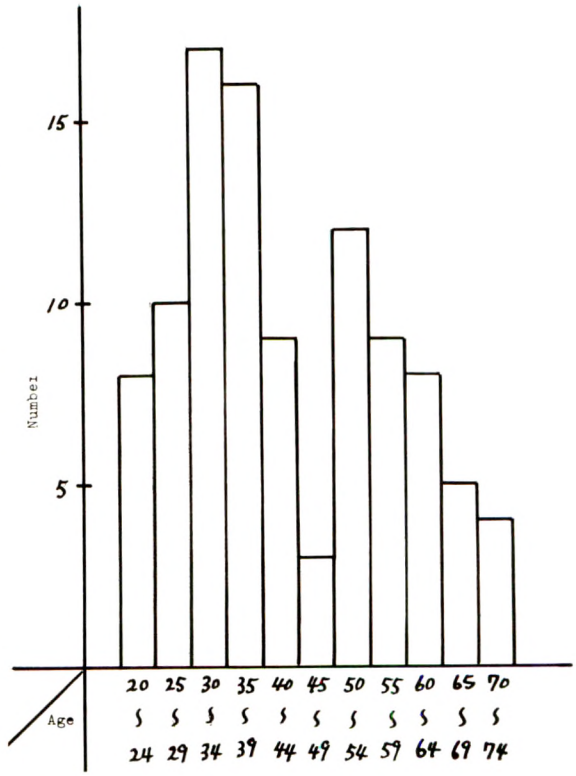


Fig. 14. Age distribution in a series of 101 cases of occlusive diseases of the artery in the lower extremity (5 cases of embolism are excluded).

TAO type. The extension of gangrene in the involved extremity of the embolic type, however, is widespread and corresponds well with the level of arterial occlusion in the present series (Fig. 26; 27; and 28, *A* and *B*), except for a case (Fig. 8) with arterial occlusion in the external iliac artery.

Seventy-six limbs were arteriographically examined in 65 cases classified as the TAO type. Gangrene in the foot was encountered in 50 per cent of the cases with occlusion in the femoral or popliteal artery and in 57 per cent of the cases with occlusion in the arteries of the lower leg or foot (Table III). Table IV demonstrates the analytic result of gangrene in the cases with occlusion in the femoral or popliteal artery. The incidence of development of gangrene in the involved extremity is extremely low in patients in whom the main arteries of the lower leg and foot are completely re-

TABLE I

THE OCCLUSIVE DISEASES OF THE ARTERY IN THE LOWER EXTREMITY

	TAO Type (Buerger's Disease)	ASO Type	Unclassified Type	Embolic Type
No. of cases	65 male 65, female 0	26 male 23, female 3	10 male 8, female 2	5 male 3, female 2
No. of examined limbs	76 right 42, left 34	33 right 16, left 17	11 right 6, left 5	5 right 3, left 2
No. of cases in which more than one limb is involved, clinically	26	20	5	0
No. of cases in which both lower limbs are involved, verified on arteriograms	11	7	1	0
Age on admission for arteriography	38.9 (21–56)	65.6 (58–75)	50.7 (25–65)	56.4 (31–69)
Age at onset of clinical signs and symptoms	35.3 (21–54)	61.0 (35–72)	46.5 (23–65)	56.4 (31–69)
Schematic illustration of 4 different patterns at the occluded stump of the artery, and incidence of the patterns in each occlusive arterial disease	I 24, II 48, III 18, IV 25	I 3, II 8, III 31, IV 2	I 5, II 2, III 2, IV 6	I 1, II 1, III 0, IV 4



TAO = thromboangiitis obliterans; ASO = arteriosclerosis obliterans.

visualized on arteriography. On the other hand, the incidence is high in patients in whom the main arteries of the lower leg and foot are completely or partially occluded.

Superficial thrombophlebitis, emphasized by Buerger as one of the cardinal signs in TAO, is extremely rare in our cases of the TAO type. In fact, there are only 5 cases with superficial thrombophlebitis in a series of 65 cases of the TAO type. Following Fisher,[6] we also believe that thrombophlebitis may be caused by infection in the gangrenous lesion and may not be one of the specific signs in thromboangiitis obliterans.

DISCUSSION

As mentioned at the beginning of this article, there are 2 practical methods for obtaining a whole-limb arteriogram. Since our experience is limited only to the "differential screen" method, a comparative study on the roentgenographic quality of both methods will not be discussed. Neither method is flawless, as roentgenographic contrast, resolution and sharpness on the

FIG. 15. (*A* and *B*) "Conical pattern" at the occluded stump of the artery in 2 different cases with thromboangiitis obliterans (TAO).

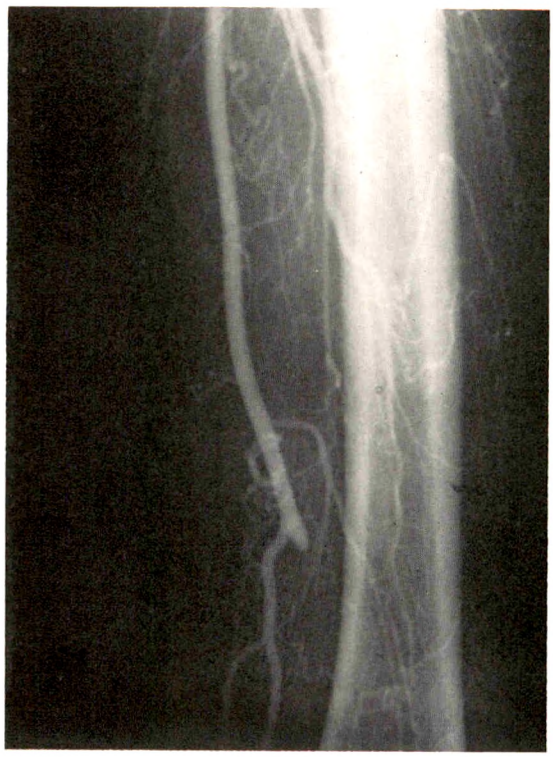
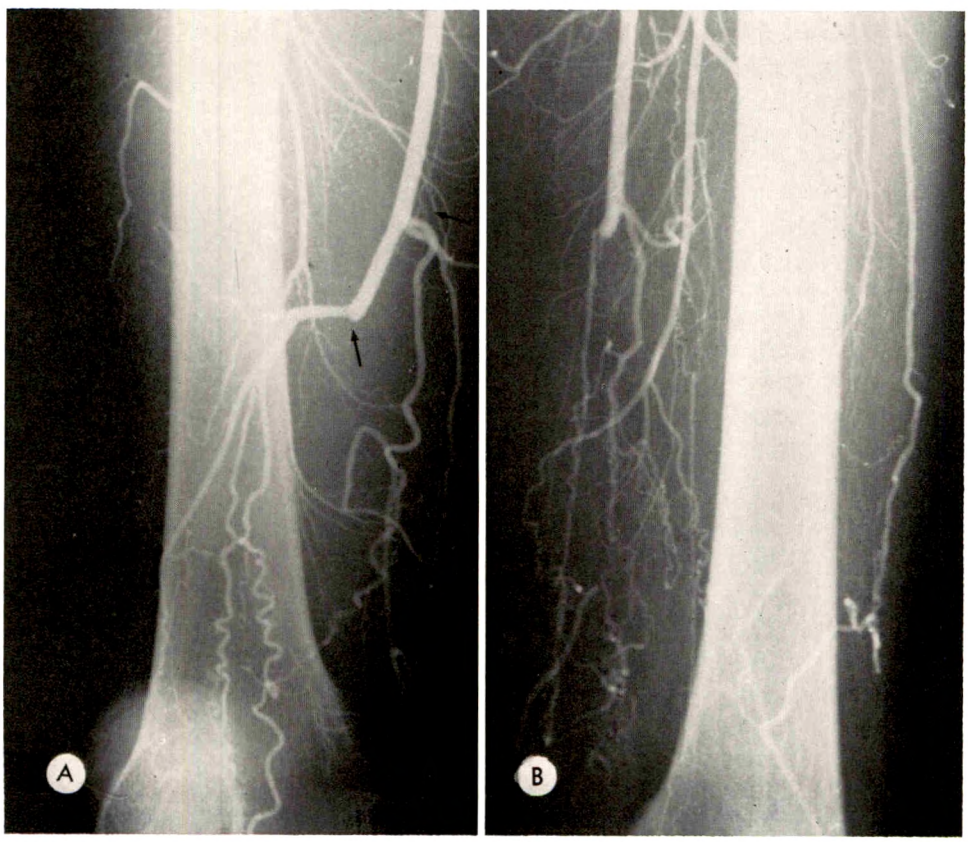


Fig. 16. Conical-shaped occlusion at the uppermost portion of the popliteal artery in a 36 year old man with TAO.

arteriogram may be influenced by the use of the differential screen or the wedge-filter.

As far as the relative usefulness of the differential screen and the wedge-filter for the plain roentgenogram of the whole lower limb is concerned, this information may be gained from an experimental study with a proper limb-phantom. A roentgenogram of the lower limb obtained with the aid of each of these accessories may have definite practical value in roentgen diagnosis, even though one compensates for roentgenographic equalization of the difference in volume at the different anatomic regions of the lower extremity.

In making a differential screen or a wedge-filter for whole-limb arteriography,



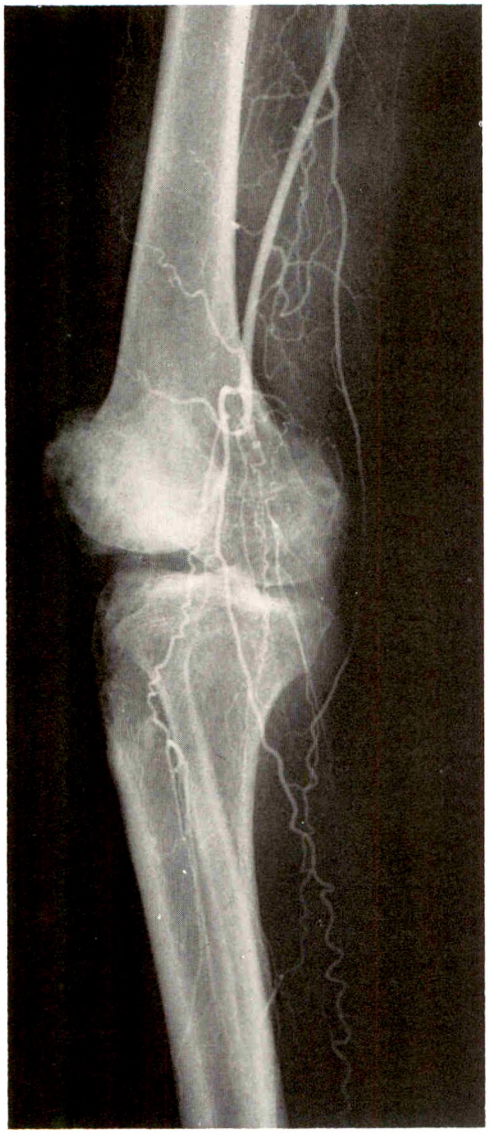


Fig. 17. "A smoothly tapering-off" at the occluded stump in a 42 year old man with TAO (age at onset: 22 years).

the following phenomenon should be taken into consideration: The contrast medium injected from the femoral artery in retrograde direction may be distributed in the capillaries, or even in the veins of the proximal portion of the lower extremity, at the time when the contrast material reaches and visualizes the arterial networks in the foot. If one applies the differential screen or the wedge-filter for a plain roentgenogram of the lower limb for whole-limb

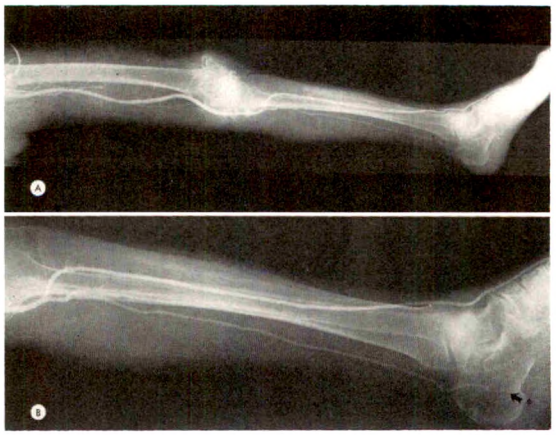


Fig. 18. (*A* and *B*) Fine ring-like contractions in both posterior and anterior tibial arteries, and occlusion in the proximal portion of the plantar artery (arrow) in a 60 year old man with gangrene in the toes of the left foot and in the fingers of both hands (unclassified type).

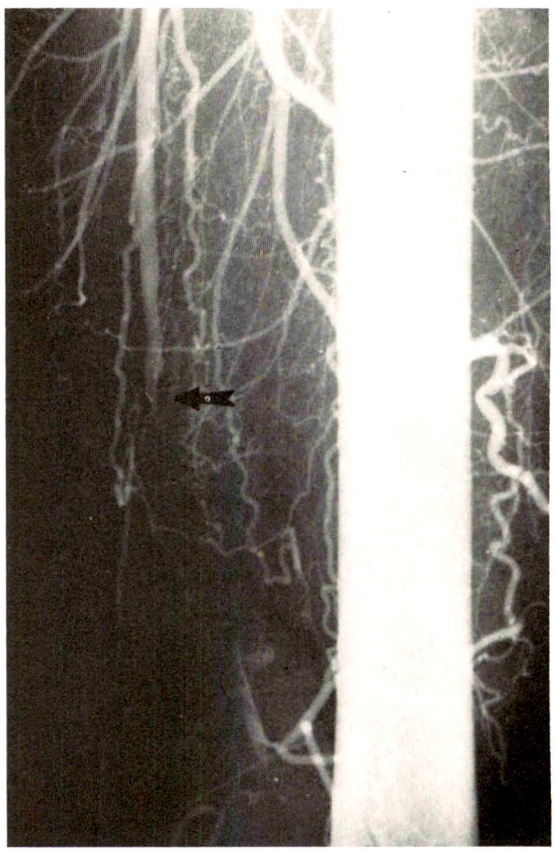


Fig. 19. An "irregularly tapering-off" in the lower portion of the femoral artery (arrow) in a 31 year old man with TAO (age at onset: 29 years).



Fig. 20. (*A* and *B*) Occlusion at the origin of the posterior tibial artery (left arrow) and an "irregularly tapering-off" in the anterior tibial artery (right arrow) in a 31 year old man with TAO (age at onset: 23 years).

arteriography, the proximal portion of the lower extremity tends to be underexposed because roentgen rays are absorbed by the radiopaque material diffusely distributed within the tissues and veins in the groin and thigh.

In order to eliminate the complex factors due to capillary or venous stains in the proximal portion of the lower limb, and to obtain seriographic information on the vascular diseases of the lower limb, we now plan to make a seriographic apparatus, as designed by Roy,[13] using 3 cassettes which contain the differential screen for the plain roentgenogram of the whole limb. In this

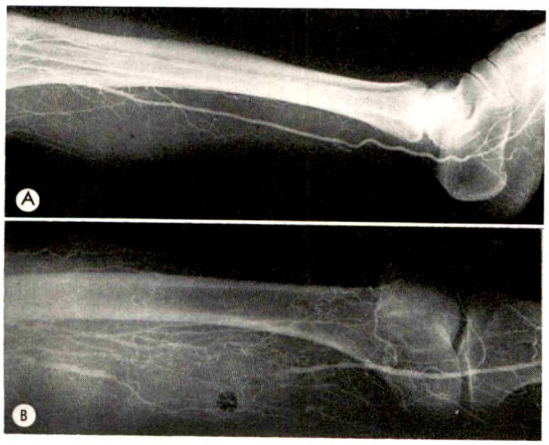


Fig. 21. (*A* and *B*) "Irregularly tapering-off" in the femoral artery in a 66 year old man with arteriosclerosis.

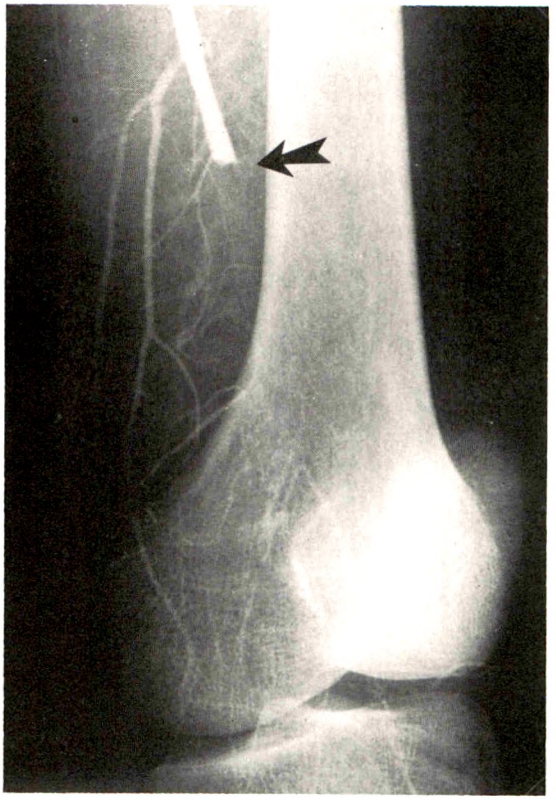


Fig. 22. "Cut-off pattern" at the occluded stump of the popliteal artery (arrow) in a 33 year old man with TAO (age at onset: 31 years).

new technique, arteriograms are made at 5, 10 and 20 seconds, respectively, after the beginning of the injection of contrast medium, instead of a single arteriogram at 20 seconds as in the present technique. Arte-

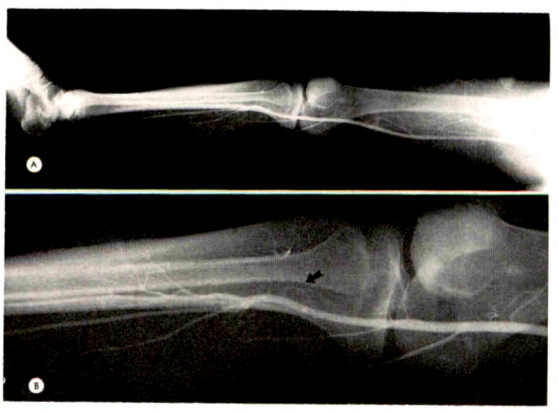


Fig. 23. (*A* and *B*) Occlusion at the origin of the anterior tibial artery (arrow) in a 37 year old man with TAO (age at onset: 35 years).



FIG. 24. The site of the arterial occlusion in a series of 65 cases of TAO (Buerger's type). Only the site of the uppermost occlusion is plotted in the cases with segmental occlusions.

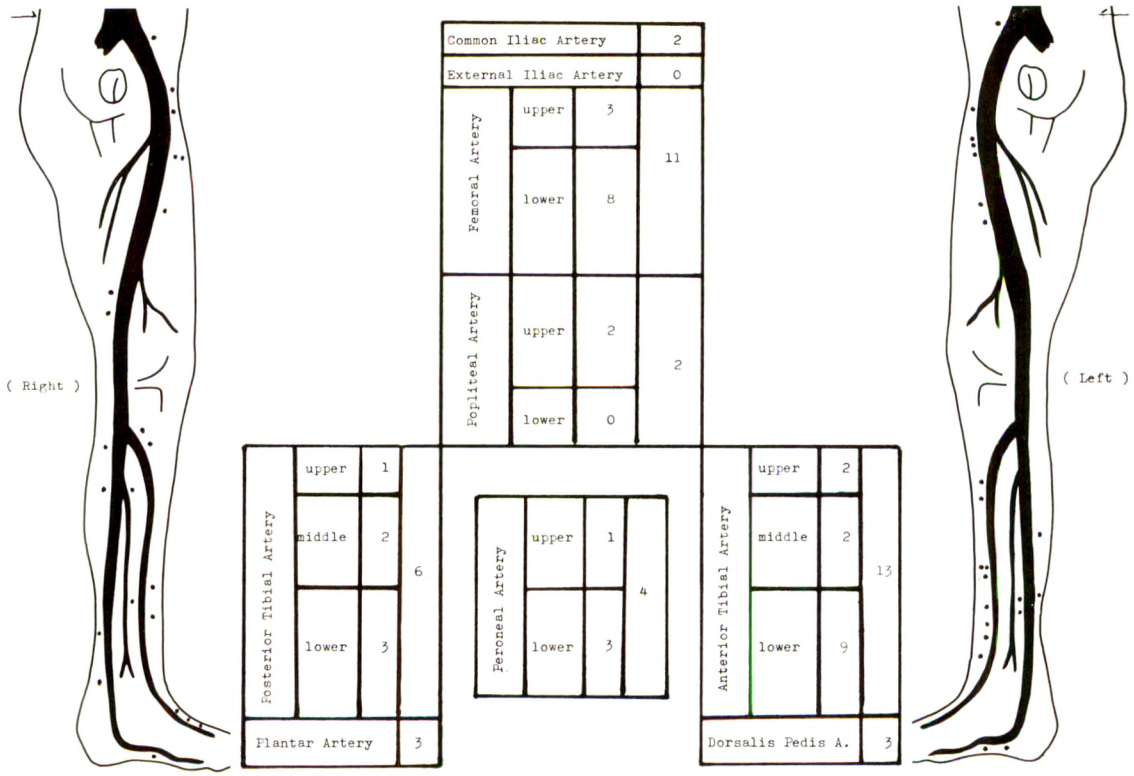


FIG. 25. The site of the arterial occlusion in a series of 26 cases of ASO (arteriosclerotic type). Only the site of the uppermost occlusion is plotted in the cases with segmental occlusions.

ries in the thigh on a 5 second arteriogram, in the knee and calf on a 10 second arteriogram and in the foot on a 20 second arteriogram can be selectively examined without being disturbed by capillary or venous stains, especially in the proximal portion of the lower limb.

SUMMARY

We performed 300 femoral arteriographies using a long cassette holding a 25×90 cm. differential screen for the whole-limb arteriography.

The differential screen proved practical for use in the arteriographic examination of the lower limb. Forty centimeters of highly concentrated contrast medium was injected into the femoral artery in the retrograde direction during a period of 20 seconds. Roentgen exposure was made immediately before the end of the injection. There were

Table II

INCIDENCE OF GANGRENE IN EACH TYPE OF OCCLUSIVE DISEASE OF THE ARTERY IN THE LOWER EXTREMITY

	TAO	ASO	Embolism
Gangrene (+)	41	5	4
Gangrene (−)	24	21	1

TAO = thromboangiitis obliterans; ASO = arteriosclerosis obliterans.

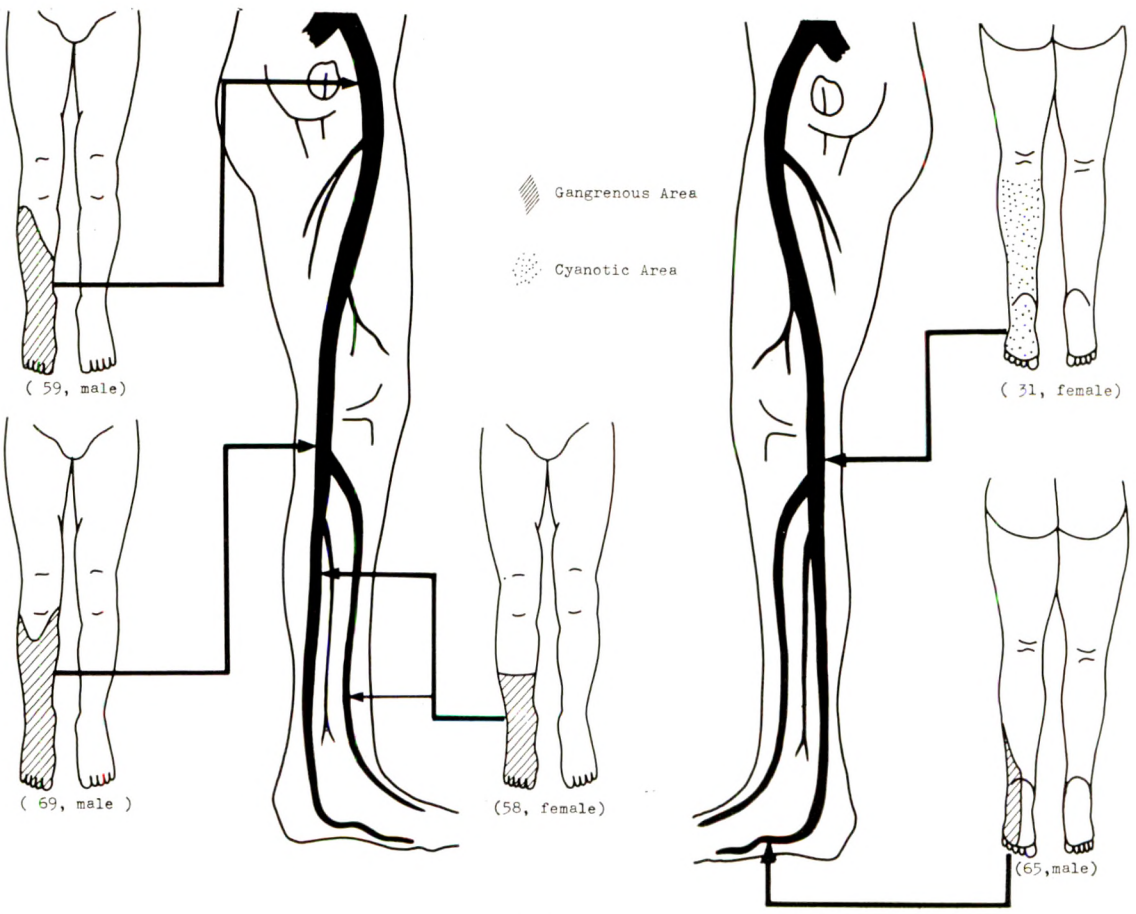


Fig. 26. Relation between the level of arterial occlusion and distribution of gangrenous and/or cyanotic area in 5 cases of embolism. Embolic attack developed during auricular flutter or fibrillation in 4 cases and following cardiac operation in 1 case.



FIG. 27. Embolic occlusion at the uppermost portion of the posterior tibial artery.



FIG. 28. (*A* and *B*) Embolic occlusion in plantar artery (black arrow). Posterior tibial artery (white arrow) is narrower in caliber than anterior tibial artery.

no complications associated with these arteriographies.

A series of 106 cases of occlusive arterial disease in the lower limb, proved by arte-

TABLE III

RELATION BETWEEN GANGRENE IN FOOT AND THE LEVEL OF ARTERIAL OCCLUSION IN A SERIES OF 65 CASES OF BUERGER'S DISEASE

76 Limbs Were Examined by Arteriography

	Gangrene (+)	Gangrene (−)
Occlusion in femoral or popliteal artery	17	17
Occlusion in the arteries of the lower leg or foot	24	18

TABLE IV

GANGRENE OF FOOT IN OCCLUSION OF FEMORAL OR POPLITEAL ARTERY

In a Series of 34 Limbs in Buerger's Disease

	Gangrene (+)	Gangrene (−)
Main arteries in the lower leg or foot revisualized by arteriography	2	12
Main arteries in the lower leg or foot completely or partially occluded	15	5

riography, is analyzed. The series consists of 65 cases of thromboangiitis obliterans (TAO), 26 of arteriosclerosis obliterans (ASO), 5 of embolism and 10 of unclassified type.

It is the author's belief that TAO in the early stage and ASO can be distinguished from each other based on purely arteriographic findings.

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CLINICAL EXPERIENCES WITH A NEW TYPE OF CONTRAST MEDIUM IN PERIPHERAL ARTERIOGRAPHY*

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MODERN contrast media for angiographic use have an over-all low toxicity, and serious adverse reactions are comparatively rare. These media are, however, concentrated salt solutions with high osmotic activity, which is, to a large extent, considered responsible for the local and general hemodynamic adverse effects known to occur on intravascular injection.

The subjective adverse effects felt by the patients in the form of pain and a sensation of heat, particularly severe in peripheral arteriography, are also related to the hyperosmotic properties of the contrast media used.

One approach to a reduction in the osmotic activity of contrast agents would be to increase their molecular size. The iodine content of the molecules must also be sufficient to give the desired contrast effect. Based on experiences with the contrast medium thorotrast in animals, Björk *et al.*[3] discussed the properties of contrast media with, among other things, lower osmotic activity than those in current use. Almén[1] published similar theoretic considerations and briefly reported preliminary animal experiments with substances which were described to be polymers of metrizoate, but the structures of the polymers were not reported. It should also be mentioned that animal experiments with certain types of dimeric contrast agents have been reported. Thus, for example, Hilal[5] and Hayes *et al.*[4] described experiments in animals with a new contrast agent consisting of a dimeric form of iothalamate which was used intravascularly. As far as we know, no clinical experiences with polymers or dimers for use in angiography have been reported previously.

Since 1963, we have been working on the synthesis and testing of polymeric, oligomeric and dimeric contrast agents in order to derive substances with lower osmotic activity and modified excretion properties. We have also aimed at structures producing minimal pharmacologic and toxicologic effects. These experiments will be published elsewhere.

From the series of dimeric contrast agents synthesized and tested, we selected the compound with the structure given in Figure 1 for extended studies and clinical tests. Our working code number for this substance in its acid form is Ph DZ 59A and the code number for its methylglucamine salt is Ph DZ 59B. An important difference from the dimeric contrast agents described earlier is the type of chain between the monomeric iodine containing units. This link was chosen because of its

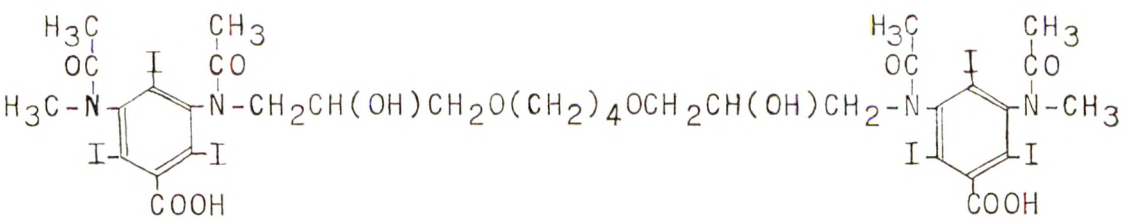


FIG. 1. Chemical structure of the new contrast compound Ph DZ 59A.

* From the Departments of Diagnostic Radiology (Head: H. Lodin, M.D.) and Clinical Chemistry (Head: A. Grönwall, M.D.), University Hospital, Uppsala and Pharmacia AB, Uppsala, Sweden.

Table I

COMPARISON OF DISCOMFORT AFTER PERIPHERAL ANGIOGRAPHY WITH 3 DIFFERENT CONTRAST MEDIA IN A DOUBLE-BLIND STUDY IN 18 PATIENTS*

Contrast Agent	Urografin 45 Per Cent	Angiografin	Ph DZ 59B
Iodine content	218 mg./ml.	209 mg./ml.	209 mg./ml.
Least discomfort	0	0	15
Most discomfort	12	1	0

* Three patients were unable to state which of the 2 media gave the least discomfort and 5 patients which of the 2 gave the most discomfort.

advantages, both from the chemical and biologic considerations. The synthesis and properties of Ph DZ 59A and B together with the results of animal experiments with this new contrast agent will be described in another paper.[2]

Compared with the contrast agents for angiography now in clinical use, this new contrast agent differs in structural details and in physical-chemical properties. In particular, the larger size of the iodine containing anion results in reduced osmotic activity and a lower diffusion constant.

Preliminary experiences with the contrast agent Ph DZ 59B in peripheral arteriography in 2 groups of patients are reported in the following.

MATERIAL AND METHODS

FIRST GROUP OF PATIENTS

This group consisted of 18 unselected patients referred for peripheral arteriography. There were 11 men and 7 women. Their ages varied from 24 to 76 years with a mean age of 48 years. In 16 patients, the injections were made in the external iliac artery, in 1 in the abdominal aorta and in 1 case in the axillary artery. In all patients, 3 different contrast media were injected with the patient and the catheter remaining in the same position for all 3 injections. The rate of the injection was the same for all 3 contrast media and the dose was 20 ml. each. The 3 contrast media used were Ph DZ 59B 51 per cent (iodine content 209 mg./ml.), urografin 45 per cent* (iodine content 218 mg./ml.), and angiografin† (diluted with saline to iodine content of 209 mg./ml.). The 3 solutions were injected randomly. An interval of at least 10 minutes between the injections permitted the subjective adverse effects to disappear and the circulatory status of the patients to be normalized. The patients' spontaneous reactions indicating pain or sensation of heat in connection with the injections were noted. After completion of the 3 injections each patient was asked to state which of the injections gave the least and which gave the most discomfort and to classify the degree of discomfort. The examiner questioning the patients had no knowledge of the order in which the 3 different contrast media were used.

Where possible the electrocardiogram and blood pressure were continuously recorded before, during and after arteriography.

Results.

Angiograms of good quality were obtained with all 3 contrast agents.

Subjective side effects. Fifteen patients reported less discomfort after the injection of Ph DZ 59B than after injections of the other 2 contrast media (Table 1). Twelve patients declared that the subjective adverse effects—sensation of heat and, in a few cases, severe pain—were most intense after the injection of urografin 45 per cent. One patient had the most discomfort after an injection of angiografin and none after

* 0.39 gm. methylglucamine diatrizoate and 0.06 gm. sodium diatrizoate per ml. Schering AG, Berlin.

† 0.65 gm. methylglucamine diatrizoate per ml., kindly supplied by Schering AG, Berlin.

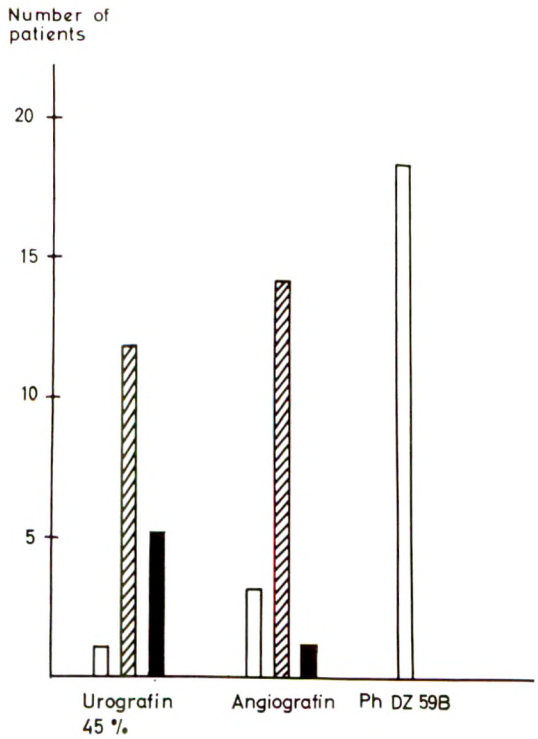


FIG. 2. Classification of subjective adverse effects (pain and sensation of heat) in 18 patients during peripheral angiography in a double-blind study. The site, rate of injection and dose were similar for all 3 contrast media. Iodine content: 218 mg./ml. for urografin 45 per cent and 209 mg./ml. for angiografin and Ph DZ 59B.
□ = slight discomfort.
▨ = moderate discomfort.
■ = severe discomfort.

Ph DZ 59B. Three patients were unable to state which of the 2 media gave the least discomfort and 5 patients which of the 2 gave the most discomfort (Table 1). The patients' classification of subjective side effects is seen in Figure 2. A statistical analysis (sign test) of the degree of discomfort showed that the subjective side effects were significantly less after Ph DZ 59B than after angiografin and urografin ($p < 0.01$), whereas the difference between urografin and angiografin was not significant.

Electrocardiographic changes. In 9 cases, satisfactory electrocardiographic recordings were obtained for all 3 contrast media. No distinct changes in the morphology of the electrocardiogram were observed with any of the 3 contrast media. After the injections there was, in most cases, a slight bradycardia followed by an increase in the heart rate lasting for 30–60 seconds. The maximal increase in heart rate was, on the average, less after injections of Ph DZ 59B than after angiografin and urografin (Table II), but the difference was not statistically significant in this small series.

Changes in blood pressure. Continuous intra-arterial recording of the blood pressure was obtained in 5 patients for all 3 injections. The increase in the heart rate was, in most cases, accompanied by a decrease both in systolic and diastolic blood pressure. There was a tendency for smaller changes in blood pressure after injection of Ph DZ 59B than after urografin and angiografin (Table II), but the material is too small for definite conclusions.

SECOND GROUP OF PATIENTS

This group consisted of 18 patients who were routinely examined by femoral artery catheterization. Twelve were men and 6 were women. Their ages varied between 18 and 69 years with a mean age of 46 years. In all patients, 3 different contrast media were injected in the femoral or iliac artery with a catheter. The patient remained in the same position for all 3 injections. The contrast media used were isopaque cerebral,* angiografin and Ph DZ 59B 57 per cent. The dose (20 ml.) and the injection rate were the same for all 3 contrast media. The same iodine content (235 mg./ml.) in all injection solutions was obtained by diluting isopaque cerebral and angiografin with water. The order in which the 3 media were injected was randomized and the examiner did not know in which order the injections had been given.

After the 3 injections had been completed, the patients were asked which of the 3 contrast media gave the most discomfort (pain and sensation of heat) and which gave the least discomfort. In addition, they were

* 0.59 gm. methylglucamine metrizoate and 0.011 gm. calcium metrizoate per ml. Nygaard & Co A/S, Oslo.

Table II

CHANGES IN HEART RATE (BEATS/MIN. INCREASE) AND BLOOD PRESSURE (MM. HG DECREASE) AFTER PERIPHERAL ARTERIOGRAPHY*

Contrast Agent	Urografin 45 Per Cent		Angiografin		Ph DZ 59B	
Iodine Content	218 mg./ml.		209 mg./ml.		209 mg./ml.	
Changes in	Heart Rate	Blood Pressure	Heart Rate	Blood Pressure	Heart Rate	Blood Pressure
Number of patients	9	5	9	5	9	5
Mean change	7	−13	8	−15	2	−8
Range	0–18	−22–0	0–18	−20–0	−3–12	−20–0

* Dose and injection rate were the same for all 3 contrast media.

asked to grade all 3 injections into 3 categories according to degree of discomfort: slight, moderate and severe. In all patients, continuous recordings of the electrocardiogram, before, during and after all 3 injections, were obtained. Whenever possible continuous recordings of intra-arterial blood pressure were also obtained. An interval of at least 10 minutes between the injections permitted the subjective discomfort felt by the patient to disappear and the blood pressure and heart rate to return to normal.

Results.

Angiograms of good quality were obtained with all 3 contrast agents.

Subjective side effects. Fourteen patients reported more discomfort after the injection of isopaque cerebral than after the other 2 media and 4 patients reported the most discomfort after angiografin. None of the patients suffered more discomfort after Ph DZ 59B than after the other 2 media. One patient experienced less discomfort after isopaque cerebral than after the other 2 media and 12 had the least discomfort after Ph DZ 59B. Five patients were unable to state which of the 2 media gave the least discomfort (Table III). When asked to grade the discomfort (slight, moderate or severe) after each contrast medium (Fig. 3), it was found that the degree of discomfort was generally most pronounced after isopaque cerebral, somewhat less pronounced after angiografin, whereas Ph DZ 59B gave the least degree of discomfort. Statistical analysis (sign test) also showed that Ph DZ 59B gave significantly less discomfort than angiografin and isopaque cerebral ($p < 0.001$), and that angiografin gave less discomfort than isopaque cerebral ($p < 0.05$).

Changes in heart rate. The mean increase in heart rate was more pronounced after angiografin and isopaque cerebral than after Ph DZ 59B (Table IV). The difference is statistically significant (analysis of variance, $p < 0.025$).

Changes in blood pressure. There was a

Table III

COMPARISON OF DISCOMFORT AFTER FEMORAL ARTERIOGRAPHY WITH 3 DIFFERENT CONTRAST MEDIA IN A DOUBLE-BLIND STUDY IN 18 PATIENTS*

Contrast Agent	Isopaque Cerebral	Angiografin	Ph DZ 59B
Iodine content	235 mg./ml.	235 mg./ml.	235 mg./ml.
Least discomfort	1	0	12
Most discomfort	14	4	0

* Five patients were unable to state which of the 2 media gave the least discomfort.

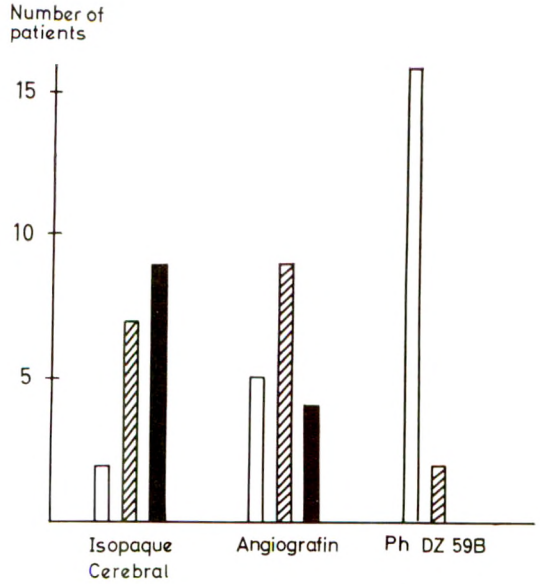


FIG. 3. Classification of subjective adverse effects (pain and sensation of heat) in 18 patients during femoral arteriography in a double-blind study. The site, rate of injection, dose and iodine content (235 mg./ml.) of contrast media were the same.
□ = slight discomfort.
▨ = moderate discomfort.
■ = severe discomfort.

tendency for a smaller decrease in systolic and diastolic arterial blood pressure after Ph DZ 59B than after the 2 other media. However, no definite conclusion can be drawn from comparative studies in only 6 patients (Table IV; Fig. 4).

One patient (No. 15 in Fig. 4) showed a very marked drop in blood pressure after the injection of angiografin into the femoral artery. He also became nauseated and vomited several times. Vomiting, nausea or allergic reactions were otherwise not seen in this series.

DISCUSSION

The quality of the angiograms obtained with the different contrast media in these 2 series was similar. This is only to be expected, since the rate of injection was the same and the iodine content identical or nearly identical for all media.

Like other contrast agents used in angiography, our substance (Ph DZ 59A) has to be used in the form of a solution of a salt of the iodine containing acid. The dependence of the adverse effects on both the iodine containing anionic moiety and the cation used is well documented in the literature. As it has been shown that methylglucamine is preferable to sodium as the cation, we have, in the clinical tests, used our contrast agent in the form of solutions of its methylglucamine salt (Ph DZ 59B). For comparison in the clinical tests, at least 1 of the other contrast agents has also been used in the form of pure methylglucamine salt.

From the 2 series presented here, it is clear that, for peripheral arteriography, Ph DZ 59B gives less subjective adverse effects in the form of pain and sensation of heat than urografin, angiografin or isopaque cerebral when compared at the same or near the same iodine concentrations. Is-

TABLE IV

CHANGES IN HEART RATE (BEATS/MIN. INCREASE) AND BLOOD PRESSURE (MM. HG DECREASE) AFTER FEMORAL ARTERIOGRAPHY*

Contrast Agent	Isopaque Cerebral		Angiografin		Ph DZ 59B	
Iodine Content	235 mg./ml.		235 mg./ml.		235 mg./ml.	
Changes in	Heart Rate	Blood Pressure	Heart Rate	Blood Pressure	Heart Rate	Blood Pressure
Number of patients	17	6	18	6	17	6
Mean change	9	−2	8	−8	2	+1
Range	−6–28	−20–20	−10–10	−30–10	−11–18	−15–25

* The dose, injection rate and iodine content/ml. were the same for all 3 contrast media.

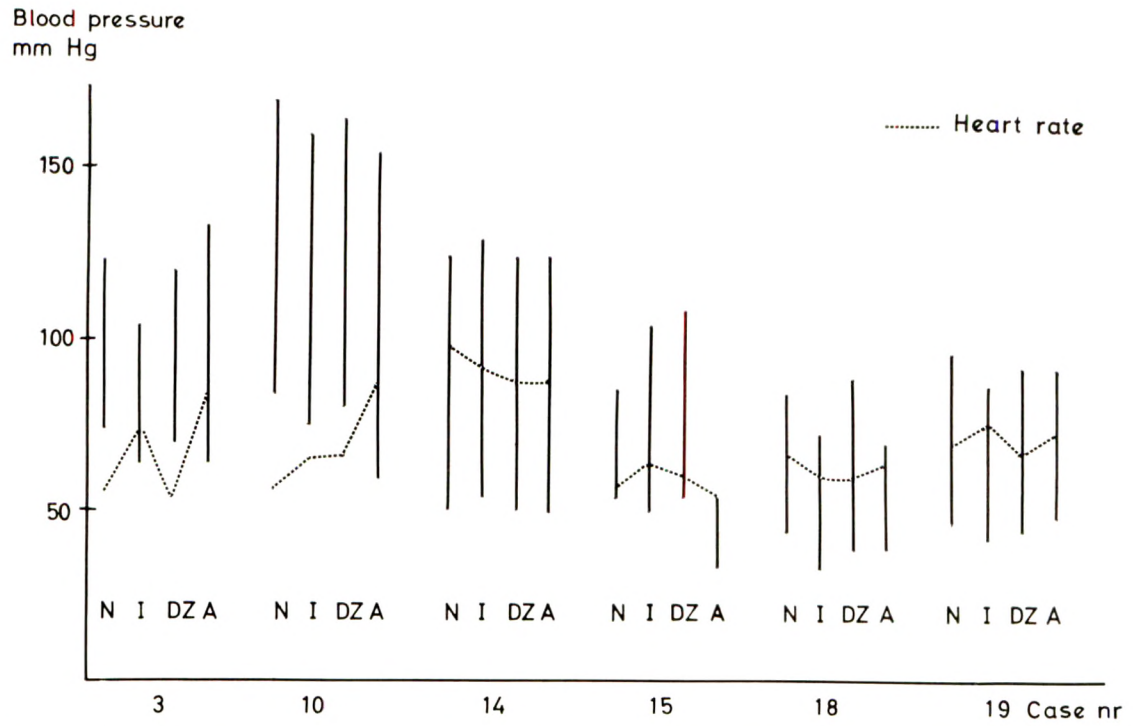


Fig. 4. Maximal changes in systolic and diastolic blood pressure and heart rate after identical injections of 3 different contrast media in 6 patients.
N = patients' normal resting blood pressure and heart rate.
I = maximal changes after isopaque cerebral.
DZ = maximal changes after Ph DZ 59B.
A = maximal changes after angiografin.

opaque cerebral also gave somewhat more discomfort than angiografin. These statistically significant differences were found at the conventional dose of only 20 ml. for iliac or femoral injections in adult patients. The rate of injection was moderate, approximately 15 ml./sec. The discomfort in the form of pain and sensation of warmth is frequently considerable in peripheral arteriography; consequently, the reduction of the subjective adverse effects with Ph DZ 59B seems to be a definite advantage over other contrast media currently in use. Both angiografin and isopaque cerebral contain methylglucamine salts. The differences in adverse effects between these 2 media and Ph DZ 59B, therefore, must to a large extent depend on the properties of the iodine containing anion. The larger size of the anion leads *inter alia* to a lowering of the osmotic effect of Ph DZ 59B and probably also to a lower rate of diffusion of the contrast agent through the cell membranes and capillary walls. The combination of properties of Ph DZ 59B is apparently sufficient to reduce the subjective adverse effects considerably.

In isopaque cerebral, there is also a small admixture of calcium metrizoate. It is possible that the calcium ions are to some extent responsible for the more pronounced subjective adverse effects experienced after isopaque cerebral than after angiografin, since it is known that calcium ions when injected for the treatment of, *e.g.*, allergic conditions, give rise to a sensation of warmth.

The methylglucamine salt solutions of contrast agents have a higher viscosity than the sodium salts at similar iodine concentrations. To keep the viscosity low, we have chosen to use solutions of moderate

concentration and iodine content. This has previously been considered a disadvantage, since a high iodine concentration was desirable for good quality angiography. With the modern roentgen apparatus, including high output generators and high output roentgen tubes, a voltage below 80 kv. can be used in nearly every angiographic study. The spectral range of the roentgen rays is then much more favorable for the absorption by iodine than with the higher voltages used 10 or 15 years ago. Therefore, the need for very high iodine content in the contrast media has diminished. Since, in most instances, a moderate lowering of the iodine content does not affect the quality of the angiograms, the use of contrast media as their methylglucamine salts is preferable, thereby taking advantage of the lower untoward effects of such compounds.

With the doses of contrast media used in these studies (about 0.2–0.3 ml./kg. body weight) more serious adverse reactions were seen in only 1 patient who showed a considerable reduction in both the systolic and diastolic blood pressure after the injection of angiografin. He was also nauseated and vomited but recovered spontaneously after 3–4 minutes.

A significantly smaller increase in heart rate after the injection of Ph DZ 59B than after injections of angiografin and isopaque cerebral was found in the second series. The number of cases where continuous recordings of the intra-arterial blood pressure were obtained was too small to permit any definite conclusions, but here also, variations in the hemodynamic status of the patients were less after the injection of Ph DZ 59B than after the other 2 contrast media. This would indicate that objectively measurable hemodynamic changes are less with this contrast medium than with the others. However, the effects on the general circulation after the peripheral arterial injection of relatively small amounts of contrast medium are generally only slight and transient, and more extensive studies are necessary before definite conclusions can be drawn. Therefore, a comparative study of the hemodynamic effects of the new contrast agent and other contrast agents during angiocardiography, thoracic aortography and cerebral arteriography is at present being conducted.

SUMMARY

A new contrast agent has been synthesized and tested in double-blind studies on 36 patients in peripheral arteriography. When compared with some other contrast media in current use at the same or near the same iodine concentration, this new agent gave angiograms of comparable quality, with significantly less subjective adverse effects in the form of pain and sensation of heat. The increase in heart rate after injection of this new agent was also less than after similar injections of the other contrast media.

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STUDIES IN THE PREVENTION OF COMPLICATIONS OF ANGIOGRAPHY*

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ANGIOGRAPHY is a valuable diagnostic procedure although there is an associated risk of mortality and morbidity from even the simplest of studies. In certain tabulated series, the mortality from angiography has ranged from 0 to 16.1 per cent and morbidity from 0 to 27.2 per cent.[5] The hazard of fatal or serious reactions to injected contrast media appears to be higher in the more severely diseased patients. The increasing proper application of angiographic procedures, particularly intra-arterial studies, to more severe, complex and extensive medical problems may increase morbidity even as advancing technical skills effect a decrease. This report represents some further observations on the nature and prevention of complications.

Tolerance studies in experimental animals given intravenous injections of radiopaque media[3] do not clarify the clinical problems of intra-arterial studies. In animals, mortality is dose-related and due to pulmonary complications with falling cardiac output, increased right ventricular pressure, pulmonary edema and hemorrhage. In clinical practice, the fatal and serious complications are not as clearly dose-related and are localized vascular problems involving primarily the central nervous system, but occasionally the kidneys and heart. Therefore, the healthy animal given intravenous injections may not be a suitable laboratory model of the patient with advanced arterial disease subjected to intra-arterial injections of contrast media.

The currently used iodinated media are known to produce temporary crenation of red cells[14] and a cytotoxic effect has been proposed to explain certain reactions.[12] Changes in the physical characteristics of blood with red cell aggregation after injection of medium have been documented in convincing detail.[4,9,13] Any of these alterations in the presence of occlusive arterial disease could explain the localized vascular pattern of complications following angiography. The abnormal red cell aggregation which develops after injection of a radiopaque medium is most readily observed under low power microscopy (50×) in the conjunctival capillary bed overlying the sclera of the eye. However, quantitation is difficult because the degree is dependent on both the aggregation tendency and local flow rates.

In disease states with tissue injury accompanied by delayed sludging, the infusion of low molecular weight dextran has been reported to be useful in preventing or reversing this phenomenon and its laboratory manifestations,[2,8] at times with clinical benefit to the patient.[7,10,11] The purpose of this study was to determine whether low molecular weight dextran given immediately prior to angiography would have any measurable effect upon the early aggregation caused by the injection of radiopaque media and/or reduce the occurrence of complications.

MATERIALS AND METHODS

All patients who had angiography from June 1965 to December 1967 were included in the study and all angiographies were done by the same staff radiologist. The patients were randomized by the sealed envelope system into 3 groups:

Group A. No preliminary hydration
Group B. Preliminary hydration with 500 cc. 5 per cent glucose in D/W intravenously in 30 minutes
Group C. Preliminary hydration with

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500 cc. 10 per cent low molecular weight dextran in 5 per cent glucose (Rheomacrodex*) intravenously in 30 minutes (average molecular weight-41,000)

All adult patients received between 50 and 75 mg. of aqueous heparin intravenously or intra-arterially during the angiographic procedure and each adult patient received a minimum of approximately 1 cc. of opaque medium per kg. body weight. At least 65 per cent of the patients had multiple injections. The majority of patients received hypaque-M, 75 (sodium and methylglucamine diatrizoates)† with lesser numbers receiving renografin-60 (meglumine diatrizoate)‡ or angio-conray (sodium iothalamate).§ Rapid injections of the medium into the aorta were made through a catheter by a Cordis injector with all delivery times less than 2 seconds.

The following measurements were made the day before the angiographic study, immediately prior to the injection of the radiopaque medium, and at 3, 10 and 30 minutes thereafter: (1) Heparinized whole blood and plasma viscosity with a Brookfield cone-plate viscometer; (2) plasma proteins by paper electrophoretic method; (3) hematocrit; and (4) total osmotic pressure by the Freezing Point Depression Method using the Advanced Osmometer.

A significant change in the condition of the patient within 30 minutes of the injection was recorded as a complication and each is listed in tabular form below. Bleeding from the vessel entered by the catheter, delayed hematoma at the puncture site, development of a false aneurysm, thrombosis at the entry site, and distal occlusion in the artery entered were considered to be complications related more to angiographic technique than to the injection of contrast media. Such technique problems appeared in approximately 4 per cent of the cases in each group and will not be considered further in this report.

RESULTS

In this period of time, 298 patients had angiographic studies. The randomization system used resulted in the following distribution:

Group A (96 patients). No hydration
Group B (106 patients). Glucose hydration
Group C (96 patients). Low molecular weight dextran hydration

The distribution of types of studies within these groups was as follows:

	Aortic Arch, Head and Neck Vessels	Abdominal Aorta and Branches, Extremities	Extremities Only	Venograms
Group A.	42 (43.7%)	42 (43.7%)	4 (4.2%)	8 (8.4%)
Group B.	58 (54.7%)	45 (42.5%)	0 (0.0%)	3 (2.8%)
Group C.	59 (61.4%)	36 (37.5%)	0 (0.0%)	1 (1.1%)

Many patients had multiple area studies. In such cases, the listing is in the column furthest to the left.

The distribution by age and sex was as follows:

	Per Cent of Male	Mean Age	Range of Age
Group A.	69/96 (71.8%)	54.16	1–80 (2 children)
Group B.	78/106 (73.6%)	57.3	18–82
Group C.	63/96 (65.6%)	59.16	15–98

* Pharmacia, Inc.
† Winthrop Laboratories.
‡ Squibb and Sons.
§ Mallinckrodt Pharmaceuticals.

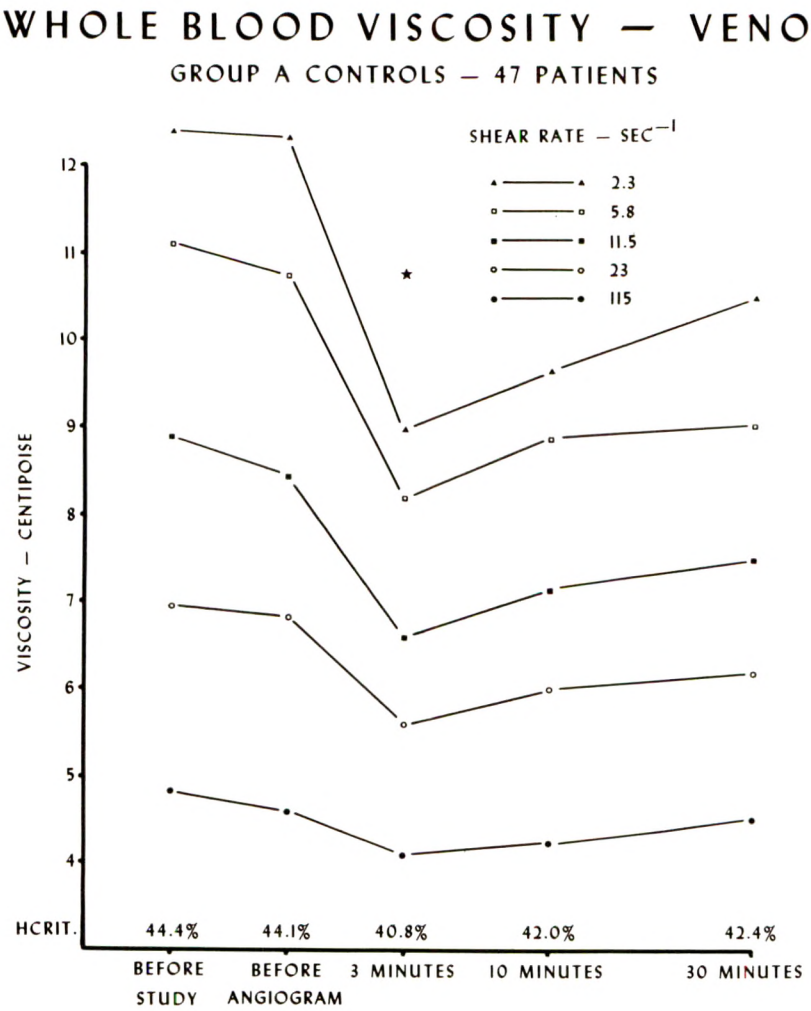


FIG. 1. Serial mean values of hematocrit and whole blood viscosity in 47 patients subjected to angiography without preliminary hydration. The "star" represents the predicted blood viscosity at a shear rate of 2.3 sec.$^{-1}$ which can be attributed to the fall in hematocrit resulting from injection of radiopaque media.

Measurements at the intervals listed showed no significant serial changes in total osmotic pressure, plasma viscosity and plasma proteins.

The combined data on hematocrit and whole blood viscosity in the first 47 cases in *Group A* are shown in Figure 1. Within 3 minutes of the injection of opaque media, a drop in viscosity at all shear rates was recorded greater than could be attributed to the hematocrit drop from the hemodiluting effect of the injected media. The predicted decrease was determined by diluting a blood sample of the initial hematocrit with its own plasma to the second hematocrit and measuring its viscosity.

The hematocrit and viscosity data on the first 49 cases in *Group B* are shown in Figure 2. A slight decrease in hematocrit with a predictable decrease in blood viscosity from the infusion of the 5 per cent glucose was noted. Again, the decrease in blood viscosity was out of proportion to the hematocrit fall when the radiopaque media were injected.

Figure 3 gives the data on the first 46 cases in *Group C*. The changes in viscosity are in direct proportion to the changes in

blood hematocrit resulting from the plasma expanding effect of both the low molecular weight dextran and the radiopaque media as predicted by actual dilution of blood samples.

The following incidence of complications was recorded:

Type of Study	Aortic Arch, Head and Neck Vessels	Abdominal Aorta	Extremities	Venograms	Total	Per Cent
Group A.	7	3	0	0	10	10.4
Group B.	6	2	0	0	8	7.6
Group C.	0	0	0	0	0	0

Excluding *Group C* in which there were no complications, the incidence by type of study was as follows:

Aortic Arch, Head and Neck Vessels	Abdominal Aorta	Extremities	Venograms
13/100 (13.0%)	5/87 (5.7%)	0/4 (0.0%)	0/11 (0.0%)

DISCUSSION

The randomization system resulted in reasonably equal numbers of patients in each group and comparable distribution of the types of studies. There were only 2 patients in the pediatrics age group, both in *Group A*. The percentage of males and the mean ages were comparable. The patient population and the studies done would therefore justify the conclusion that the 3 groups were equivalent.

The coincidence of visible sludging and viscosity decrease has been observed now in more than 100 patients. The disagreement of this observation with Dintenfass' statement that aggregation is accompanied by an increase in blood viscosity[6] must be due to the instrumentation used.

In animal studies in our laboratories, visible sludging in the conjunctival capillary beds and a marked fall in whole blood viscosity out of proportion to the decrease in hematocrit, was consistently observed within 3 minutes of intra-arterial injections of the radiopaque medium. Neither of these findings were observed when the animals received 1 gm./kg. of low molecular weight dextran before the injection. In the patient studies, routine capillary observation was not done because of technical difficulties and unreliable grading of the observations.

It was hoped that a more reliable index would be serial blood viscosity measurements. There were many instances of marked divergence of viscosity and hematocrit and the accumulated data (Fig. 1 and 2) clearly reveal this tendency in *Group A* and *Group B*. This divergence is notably absent in *Group C* (Fig. 3). The relationship of the coincident changes in blood viscosity and visible aggregation is not established by these data. The presence of significant aggregation downstream in the arterial system can only be presumed from these studies on venous blood. The failure to demonstrate any significant change in total osmotic pressure measurements at the intervals samples does not rule out significant, temporary red cell crenation. Measurement of plasma viscosity with the Brookfield viscometer was too unreliable to justify efforts at interpretation beyond the fact that no serial changes were noted. Absence of serial changes in plasma proteins may be the result of the sampling period. These findings indicate that the aggregation occurring in angiography is not the delayed type reported

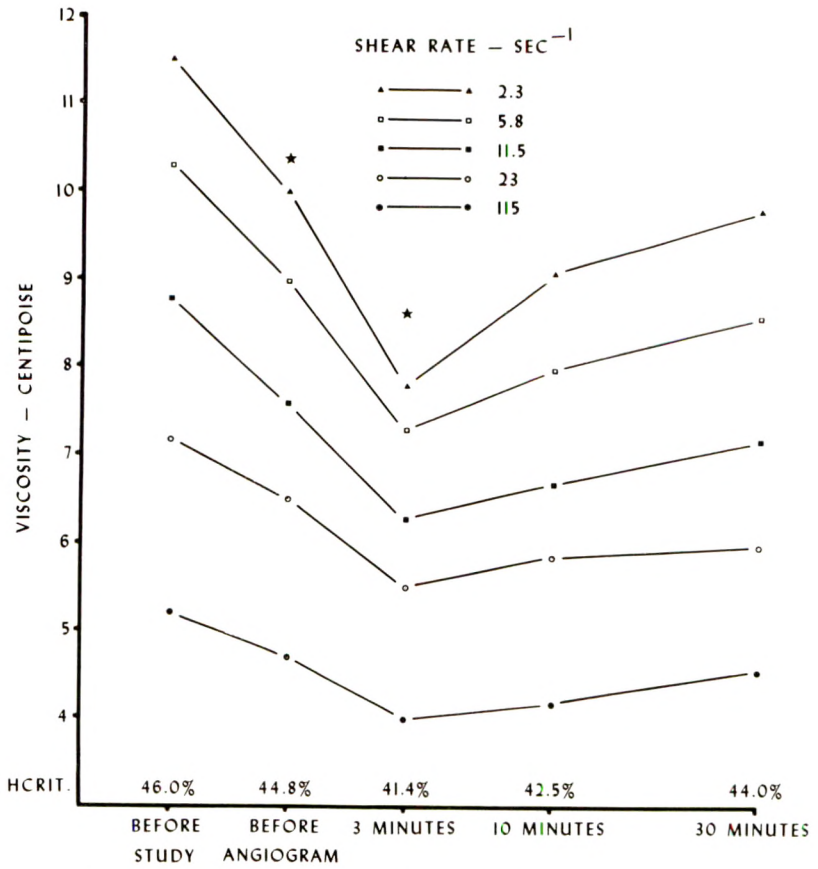


Fig. 2. Serial mean values of hematocrit and whole blood viscosity in 49 patients subjected to angiography after preliminary hydration with 5 per cent glucose in distilled water. The "stars" represent predicted changes in blood viscosity at a shear rate of 2.3 sec.$^{-1}$ due to the fall in hematocrit resulting from the glucose infusion and injection of radiopaque media.

with tissue injury, appearing in 8–24 hours and associated with increasing levels of fibrinogen.[1] The immediate aggregation observed would be more likely the result of the direct effect of the media on the red cell membrane, its protein envelope, or circulating plasma proteins. As such, it resembles more the aggregation produced by snake venom, thromboplastin, bruised blood and high molecular weight dextrans. The prompt appearance of complications in *Group A* and *Group B* permits a speculative relationship to the aggregation phenomenon.

The hematocrit and viscosity changes noted with low molecular dextran infusion correspond to the plasma expanding properties of this material. All groups showed predictable hematocrit and viscosity decreases with injection of the markedly hypertonic opaque media. The recovery trend within 30 minutes was probably due to renal excretion of part of the injected media with some decrease in plasma volume. An apparent full return to pre-injection levels in *Group C* is undoubtedly due to the simultaneous excretion of both the media and the low molecular weight dex-

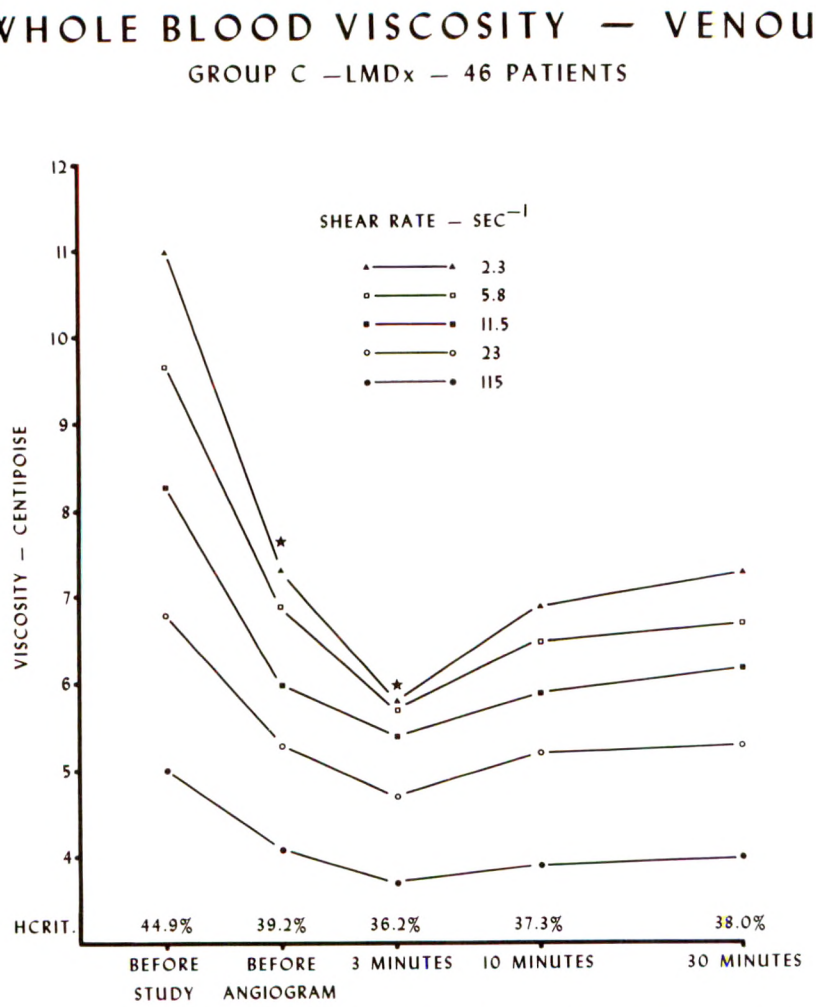


FIG. 3. Serial mean values of hematocrit and whole blood viscosity in 46 patients subjected to angiography with preliminary hydration with low molecular weight dextran. The "stars" represent predicted changes in blood viscosity at a shear rate of 2.3 sec.$^{-1}$ due to fall in hematocrit resulting from the dextran infusion and injection of radiopaque media.

tran. The rapid preliminary infusion of 5 per cent glucose had some apparent plasma expanding effect as suggested by the hematocrit decrease. Therefore, it was difficult to attribute the protective effect of the low molecular weight dextran to hemodilution alone. The plasma volume expansion from both low molecular weight dextran and radiopaque media has been confirmed by serial plasma volume measurements in animals in our laboratories.

In analyzing the complications by the type of study, excluding *Group C*, there were 13 out of 100 head and neck studies (13.0 per cent); 5 out of 87 abdominal/renal/extremity studies (5.7 per cent); 0 in 4 extremity studies (0.0 per cent); and 0 in 10 venograms (0.0 per cent). This occurrence conforms to the accepted hazard gradient but may also indicate that the cerebral tissues are more graphic reflectors of temporary injury or ischemia than the viscera or the extremities.

Thirteen of the eighteen complications occurred with the initial injection of the radiopaque media, which fails to support a dose relationship.

Comparing the statistics by the method

TABLE I

TABULATION OF THE COMPLICATIONS

Patient No.	Age (yr.)	Opaque Medium	Vessels Injected	Complications
Group A				
1	55	60 cc. Hypaque-M, 75	Retrograde, left subclavian artery	Left facial paralysis in minutes; clear in 24 hours
10	57	60 cc. Hypaque-M, 75	Aortic arch	Partial aphasia in 2 minutes; cleared in several hours
19	59	80 cc. Renografin-60	Abdominal aorta	Within 20 minutes, apneic, comatose with bradycardia. Died in 5 days
20	55	60 cc. Angio-Conray	Aortic arch	Immediate aphasia; cleared in 24 hours
42	36	50 cc. Angio-Conray	Abdominal aorta	Gradual development of findings of transverse myelitis; complete recovery in 6 months
43	62	90 cc. Angio-Conray	Aortic arch (60 cc.) Innominate artery (30 cc.)	In 2 minutes, general convulsions with left hemiplegia; coma for 4 hours; incomplete recovery in 36 hours
45	57	60 cc. Angio-Conray	Aortic arch	In 15 minutes, partial aphasia; clearing in 2 hours
46	54	120 cc. Angio-Conray	Aortic arch	Immediate generalized convulsions with diffuse paresis after second 60 ml. injection; cleared in 24 hours
91	52	60 cc. Hypaque-M, 75 30 cc. Renografin-60	Aortic arch (60 cc.) Left subclavian artery (30 cc.)	Immediate decrease in responsive state; semicomatose in 6 hours; dysphasia and dysnomia for 2 weeks
95	44	155 cc. Hypaque-M, 75	Abdominal aorta	Rapidly developed pulmonary edema, hemoptysis, pleuritic chest pain, response to treatment in 1 week
Group B				
2	65	60 cc. Hypaque-M, 75 80 cc. Renografin-60	Aortic arch (60 cc.) Innominate artery (40 cc. × 2)	Progressively unresponsive after procedure with fixed right hemiplegia
3	57	60 cc. Hypaque-M, 75 4 cc. Renografin-60	Aortic arch (60 cc.) Innominate artery (4 cc.)	Within 5 minutes, left facial weakness followed by paresis of left index finger and thumb; almost total clearing in 36 hours
17	65	60 cc. Hypaque-M, 75 50 cc. Renografin-60	Aortic arch (60 cc.) Right carotid artery (25 cc. × 2)	Progressively unresponsive with coma 4 hours after angiography; semi-responsive in 24 hours with left hemiparesis; almost total recovery in 48 hours

TABLE I (*Continued*)

Patient No.	Age (yr.)	Opaque Medium	Vessels Injected	Complications
31	66	120 cc. Hypaque-M, 75 15 cc. Renografin-60	Abdominal aorta, right renal artery (15 cc.)	Infarction of inferior half of right kidney noted on late roentgenograms with transient uremia; later bleeding diathesis with cardiac failure; adequate response to transfusion and cardiac drugs
41	60	4 cc. test dose Hypaque-M, 75	Aortic arch	Immediate unresponsiveness progressing to deep coma; recovery with fixed left hemiplegia
42	45	90 cc. Hypaque-M, 75	Aortic arch (60 cc.) Innominate artery (30 cc.)	Immediately after procedure left sided convulsions, followed by coma and left hemiplegia; recovery in 24 hours
71	56	120 cc. Hypaque-M, 75	Aortic arch	After procedure, patient complained of blurred vision; studies showed a large permanent central field defect on right
94	65	180 cc. Hypaque-M, 75	Aortic arch (60 cc.) Abdominal aorta (60 cc. × 2)	Abdominal pain and nausea immediately after procedure. At time of surgery next day for his femoral occlusion, 10 cm. of gangrenous small bowel removed because of mesenteric artery thrombosis
Group C		No complications		

of the differences in proportions, the probability that the difference in incidence of complications between *Group A* and *Group C* (10.4 per cent *vs.* 0 per cent) would occur by chance alone would be less than 0.0025, which is highly significant. By the same method, the probability that the difference between *Group B* and *Group C* (7.6 per cent *vs.* 0 per cent) would occur by chance alone is less than 0.01, also highly significant. The probability that the difference in complications between *Group A* and *Group B* (10.4 per cent *vs.* 7.6 per cent) would occur by chance is 0.5, which is not significant, and shows that hydration alone has no prophylactic value. Combining *Group A* and *Group B* and comparing with *Group C* (8.9 per cent *vs.* 0 per cent), the probability of this difference occurring by chance alone is less than 0.005, which is statistically significant. These data permit the conclusion that low molecular weight dextran given as a 10 per cent solution in 5 per cent glucose, in a dose which averages slightly less than 1 gm./kg. body weight, immediately prior to angiographic studies significantly reduced the incidence of complications.

SUMMARY

1. The 298 patients subjected to angiography were randomized by the sealed envelope system into 3 groups.

2. *Group A* received no preliminary hydration. *Group B* received 500 cc. 5 per cent glucose in distilled water immediately prior to angiography. *Group C* received 500 cc. 10 per cent low molecular weight dextran in 5 per cent glucose immediately prior to angiography.

3. Serial measurements of venous blood hematocrit and viscosity showed changes consistently associated with abnormal red

cell aggregation in *Group A* and *Group B* only.

4. No statistically significant difference in the incidence of complications was noted between *Group A* and *Group B*, indicating that hydration alone has no prophylactic value.

5. Statistically significant reduction in the incidence of complications was noted in *Group C*, when compared with either *Group A*, *Group B*, or *Group A* and *Group B* combined.

6. Low molecular weight dextran given intravenously as a 10 per cent solution in 5 per cent glucose immediately prior to angiography significantly reduced the incidence of complications from these procedures.

7. The infusion program described produced no complications or reactions.

8. Pre-angiographic infusion of low molecular weight dextran can be recommended as a safe and effective means of reducing the hazards of arteriography.

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Since this paper was submitted for publication, 319 additional patients have been subjected to arteriography. Each received pre-angiographic infusion of low molecular weight dextran as outlined in the report.

A reaction occurred in 1 of these 319 patients—a 57 year old man who developed myocardial infarction and ventricular fibrillation approximately 30 minutes following transbrachial injection of the right subclavian artery. The patient was still on the examining table at the time of his attack and, with defibrillation and appropriate supportive therapy, he recovered. Six months later, this patient had an uncomplicated transfemoral arch study with additional left subclavian artery catheterization following pre-angiographic infusion of low molecular weight dextran.

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KETAMINE: A NEW ANESTHETIC FOR USE IN PEDIATRIC NEUROROENTGENOLOGIC PROCEDURES*

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IT HAS been our practice to use general anesthesia during neuroroentgenologic procedures in children under 16 years of age. In a previous study[1] we found several cases of unsuspected pulmonary collapse due to unintentional endobronchial intubation which occurred with what was considered to be a properly placed endotracheal tube. Such endobronchial intubation is a misadventure difficult, if not impossible, to detect clinically in the infant and small child. Reports of the effectiveness and safety of ketamine* anesthesia for pediatric surgery[4] prompted us to explore the feasibility of its routine clinical use for neuroroentgenologic procedures in this age group.

The anesthetic properties of the compound ketamine (2-[o-chlorophenyl]-2-methylamino cyclohexanone HCl [CI-581]) in man have been described.[2,5] It was used with success for pneumoencephalography soon after its introduction into clinical use.[2]

METHOD OF ANESTHESIA

Premedication. Scopolamine or atropine is given parenterally in the customary manner. The only other medication used prior to induction, and then only in those patients exhibiting nasal congestion, is topical phenylephrine hydrochloride 0.125 per cent.

Anticonvulsant medications are usually withheld prior to the procedure on the day of the study.

Preanesthetic Preparations. Intravenous infusions are started whenever possible. Ace bandages are applied to the legs prior to sitting the patient upright for pneumoencephalography. A digital pulse monitor, a blood pressure cuff over the brachial artery, and a precordial stethoscope are used to monitor the patient's cardiorespiratory functions. Rectal temperature is monitored in infants. Warming pads are used when necessary.

Ketamine Anesthesia. The induction dose may be given intravenously or intramuscularly. In infants, small children, and uncooperative older children, the induction dose may be given intramuscularly as the first step prior to attempts to start the intravenous infusion. The induction dose when given intravenously is 1 to 2 mg./kg.; and when given intramuscularly, 8 to 12 mg./kg. The onset of complete surgical anesthesia is established about 30 seconds after completion of the intravenous injection or about 6 to 12 minutes after intramuscular administration. Complete analgesia is assumed by the lack of reaction to various pain inducing procedures. With intravenous administration, anesthesia lasts 5 to 10 minutes, and with intramuscular, 30 to 60 minutes, depending upon the age, physical state of the patient, and the nature of the procedure.

Table 1 lists the per cent of patients receiving the drug by each of the routes.

Reinforcing doses are given as required. These doses may range from 10 to 50 per cent of the induction dose. In those cases maintained by the intravenous method, the first few reinforcing increments are given

* Ketamine—Ketalar (Parke-Davis).

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empirically within a few minutes of the induction dose, inasmuch as the effect of the drug when given intravenously is so brief in duration. Intravenous reinforcing doses will usually be required every 10 to 15 minutes. Those patients receiving reinforcing doses by the intramuscular route will usually not require more frequent dosage than at hourly intervals. The indication for reinforcing doses is usually movement that interferes with the procedure.

Increased muscle tone was commonly seen following induction with ketamine. Frequently this is pronounced when the induction dose is inadequate, but the tone of the muscles can usually be reduced with additional ketamine. Later on, if additional doses of ketamine do not control movement, diazepam* is used in children over 12 years of age, in doses up to 1 mg.

It is important that the antisialagogue effect of the premedication be obvious to prevent obstructing secretions from forming in the airway. If salivation is excessive, one-third to one-half of the dose of the belladonna drug given as a premedication is administered. These augmenting doses are adequate in controlling salivation.

If spontaneous respiration is considered inadequate at any time the method of anesthesia is converted to that of endotracheal inhalation.

MATERIAL

Since July 1967, ketamine anesthesia has been used routinely in children undergoing pneumoencephalography or cerebral angiography unless contraindicated.

Patients in whom ketamine is absolutely contraindicated are those with hypertension, possible cerebrovascular accident, cardiac decompensation, or those in whom upper airway manipulations are contemplated.

During pneumoencephalography and cerebral angiography, it is at times necessary to position the patients with their necks acutely flexed. The effect of this posture upon the patency of the upper airway should be evaluated during the preoperative appraisal of the patient by having him assume this position while he is awake. If obstruction of the upper airway at such a time is revealed, ketamine should not be used. The presence of secretions in an otherwise normal airway also constitutes a relative contraindication to the use of ketamine.

Table I

Distribution of Patients as to Route of Administration

Route	Intravenous (per cent)	Intramuscular (per cent)	Intravenous and Intramuscular (per cent)
Pneumoencephalography	30	15	55
Carotid angiography	50	15	35

To date there have been 126 pneumoencephalographies and 59 cerebral angiographies performed using ketamine anesthesia. The age range of these patients is shown in Figures 1 and 2.

RESULTS

Anesthesia was considered satisfactory in all but 5 of the patients. These studies could not be completed with ketamine anesthesia because of ventilatory inadequacy.

The patients in whom successful ketamine anesthesia was not accomplished were: (1) A 3 month old infant who developed an episode of intermittent breath-holding on induction which lasted several minutes and was associated with bradycardia. Although recovery was prompt the case was discontinued; (2) a 3 year old child who developed intermittent but persistent rigidity and breath-holding during induction. Muscular relaxation could not be obtained in this patient with additional ketamine. The child was intubated with mus-

* Diazepam—Valium.

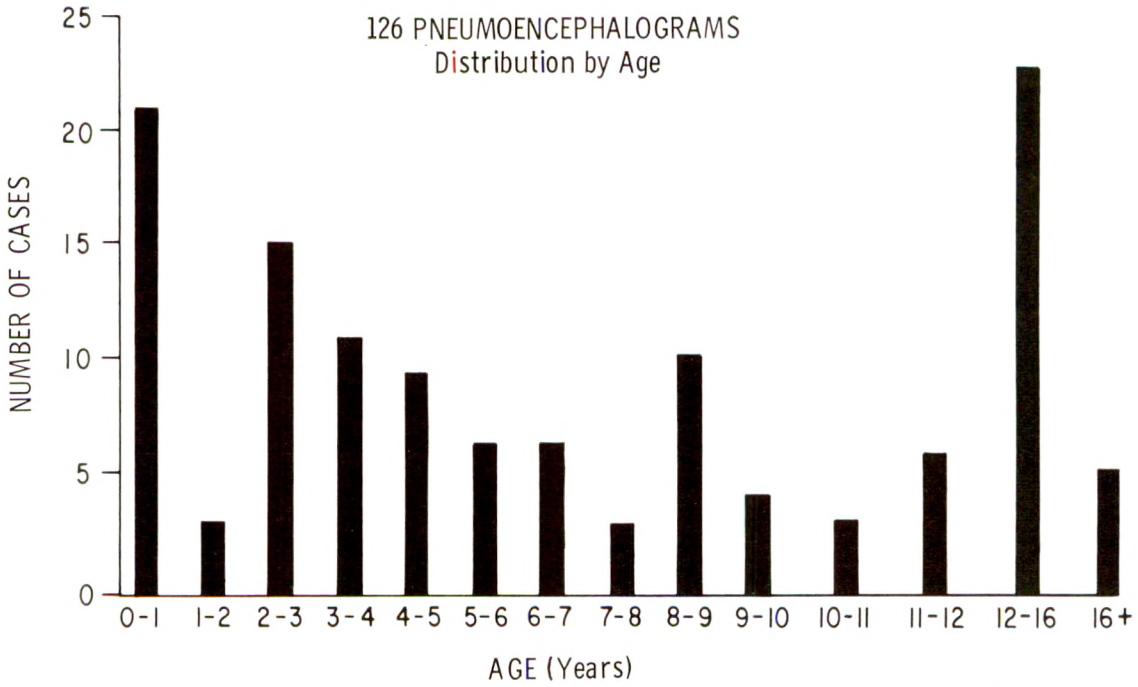


FIG. 1. Age distribution of patients in 126 pneumoencephalograms obtained using ketamine anesthesia.

cular relaxation afforded by succinylcholine and the procedure completed satisfactorily with an inhalation method; (3) a 6 week old infant who displayed breath-holding which was probably precipitated by the presence of pharyngeal secretions. One month later this infant was given satisfactory ketamine anesthesia for pneumoencephalography; (4) a 9 month old child in whom, following induction, the airway was noisy and partially obstructed. This child was noted to have thick secretions in the lower airway prior to induction and ketamine anesthesia should not have been attempted. The patient was intubated and pneumoencephalography completed satisfactorily with inhalation anesthesia; and (5) a 10 year old child with pharyngeal muscle weakness secondary to a

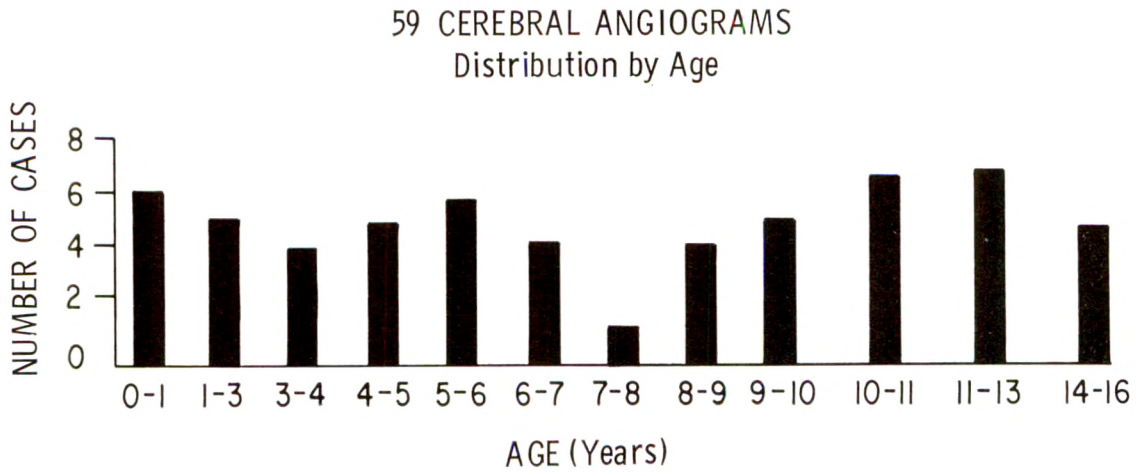


FIG. 2. Age distribution of patients in 59 cerebral angiograms obtained using ketamine anesthesia.

brain stem tumor. This patient developed upper airway obstruction with acute neck flexion, and had to be intubated and carried on inhalation anesthesia for completion of the cerebral angiography. The upper airway obstruction in this child was due to relaxation during anesthesia of his already weak pharyngeal musculature. This was enough to occlude the nasopharynx when the neck was flexed for the half-axial projection. The muscles that in the awake state keep the upper airway patent seem generally to be minimally relaxed during ketamine anesthesia. But in this case relaxation, even to that slight extent, was enough to obstruct his respiration.

About 10 per cent of the patients manifested muscular movements of the extremities.

Several patients were noted to produce excessive saliva which they were seen to swallow or effectively extrude from their mouths with coordinated movement of their lips.

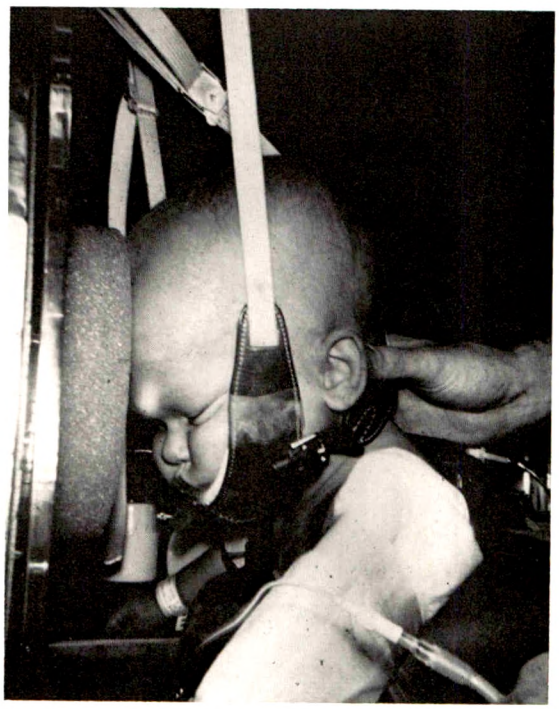


Fig. 3. This type of head suspension suspends the patient's head by the chin, thereby forcing the mouth closed so that the nose becomes the only airway.

DISCUSSION

No serious adverse effects were noted during anesthesia and no complications occurred following the procedures. The anesthesia for the majority of the cases was smooth and completely uneventful. No local tissue reaction was observed following intramuscular or intravenous injection of ketamine.

Stability of the cardiovascular and respiratory systems was impressive. As a precautionary measure against hypotension during the upright phase of the pneumoencephalography, ace bandages were wrapped around the lower extremities of the patients prior to sitting them upright. Rarely, transient hypotension occurred when gas was injected into the subarachnoid space. No interference with respiration, however, was clinically discernible in these rare cases of hypotension. A slight pressor effect upon the circulation was noted in most patients immediately after induction. Hypertension causing concern was never seen. The number of patients continuing to manifest the pressor effect with reinforcing doses, however, was seen to decrease after the first hour for those in the sitting position and slightly later for those in the recumbent position.

Respiration appeared little affected by ketamine. However, respiration may be compromised in infants and small children if the soft tissues of the suprahyoid region are unavoidably crowded into the oralpharyngeal cavity when the head is suspended by a leather strap under the chin during the upright phase of pneumoencephalography. In the past, most encephalographic devices have supported the head by the chin, either from below or suspended (Fig. 3). Radberg[6] designed a cap for head suspension which we have adopted for infants and small children. When using the cap suspension, respiration is not impeded, and easy access to the mouth is allowed because the cap is taped to the forehead and neck without restraining the

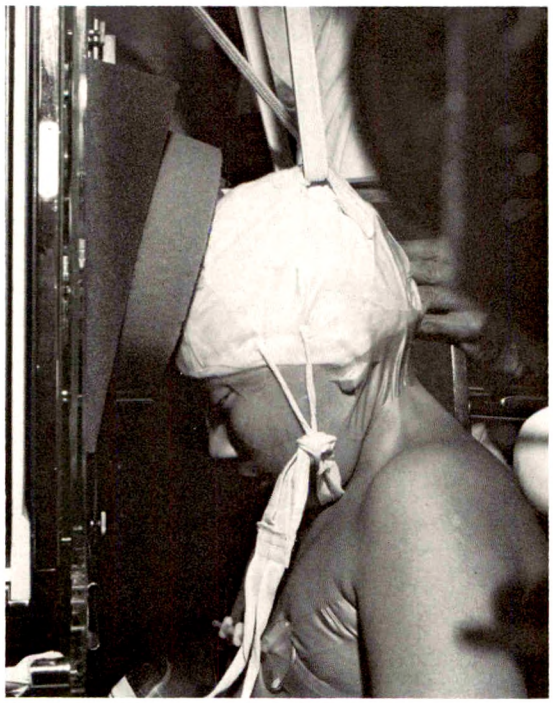


FIG. 4. When the cap suspension device is used, the chin strap is tied loosely and the mouth is not forced closed so that respiration is not impaired.

chin (Fig. 4). The loosely tied cloth chin strap serves only as an emergency catch in case the head becomes untaped. The nasal decongestant used prior to induction was especially useful in those patients whose heads were supported with a sling under the chin, making the nasal passages the only airway.

The reflexes of the respiratory tract appear exaggerated during ketamine anesthesia, and the presence of secretions about the larynx may cause reflex laryngospasm. Pharyngeal secretions with reflex breath-holding were the cause of at least two of the anesthetic failures in our series.

The muscular movements that occurred in a small per cent of patients were purposeless, and were most often limited to the extremities, only occasionally involving the head. These movements usually could be easily controlled by restraining with tape.

Blood gas analyses were performed during carotid angiography on 33 patients using blood obtained from the arterial catheter while the patients were breathing room air. The range of variation in blood gas values among the patients was rather narrow, and the average of each group of values was within physiologic limits for patients breathing room air (Table II).

Two aspects of the anesthetic state produced by ketamine became evident: a short lasting analgesia on one hand, and a longer lasting period of unconsciousness or "coma" on the other. This latter state often resembled familiar "very light anesthesia." That is, with induction both profound analgesia and coma were rapidly accomplished. Analgesia faded first while coma persisted and then it, too, faded, but much more slowly. An additional dose of ketamine thereupon would augment both aspects of the anesthetic state but it would not proportionately prolong the coma. There were, however, examples where the reverse to this was evident, namely, several patients were completely lucid, and had complete analgesia. Profound analgesia is not required during a large portion of the time necessary to perform the neuroroentgenologic procedures so that the patient can be maintained in the "lightly anesthetized" state in the intervals between injections or other pain-producing maneuvers.

There is apparently perfect compatibility clinically between ketamine and other anesthetic agents, and conversion from ketamine anesthesia to anesthesia with other agents can be done easily and quickly.

The recovery period following ketamine anesthesia was variable. Several patients were awake before the procedure had been

TABLE II

BLOOD GAS STUDY

Total Average for 33 Patients	
pH	7.342
P_{O_2}	96.064
P_{CO_2}	42.974
S_{O_2}	91.280
Hct.	34.438

completed. Such patients were indifferent to the concluding maneuvers. Many of the patients were awake within the first hour of the recovery period. Most awakened gradually and quietly. The length of time to recovery was not necessarily directly related to total dose used. Recovery from prolonged ketamine anesthesia was generally delayed by the slow return of mental clarity.

All patients who could be interrogated had amnesia for the period of anesthesia and almost all of them had amnesia for the recovery period.

In the recovery room support of respiration or circulation was never necessary.

Psychotomimetic effects that have been reported in adults during emergence from ketamine anesthesia [2,7] were not seen in this group of patients. The absence of such effects in pediatric patients has been reported by others.[3] Diplopia was noted occasionally but it was evanescent. Vomiting during the recovery was not seen following cerebral angiography. Vomiting did occur following pneumoencephalography but the danger of aspiration was reduced because the activity of the pharyngeal reflexes was not reduced by ketamine anesthesia.

SUMMARY AND CONCLUSION

Among the advantages of ketamine anesthesia over other types of general anesthesia for neuroroentgenologic procedures are the absence of respiratory and circulatory depression and the rapidity with which the anesthetized state can be achieved. These characteristics obviate the need for endotracheal intubation and assisted respiration. The absence of anesthetic appliances facilitates the technical aspects of the procedure.

Ketamine has proved to be an excellent anesthetic agent for use during neuroroentgenologic procedures in children.

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A NEW HEAD POSITIONING DEVICE FOR CEREBRAL ANGIOGRAPHY AND PNEUMOENCEPHALOGRAPHY*

By K. FRANCIS LEE, M.D.†
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IT IS a known fact that accurate positioning of the head and proper angulation of the roentgen-ray tube are essential to produce a cerebral angiogram or pneumoencephalogram of good quality.

It is the purpose of this paper to describe a head positioning device which has been proved to be useful in accurate positioning of the head.

METHOD

The head positioning device (Fig. 1) is mounted on the patient's head by means of the adjustable median supporting bar and ear plugs. The median bar and ear plugs have adjustable coil springs so that the unit is snugly but firmly attached to the patient's head during the positioning. In order to double check the position of the head

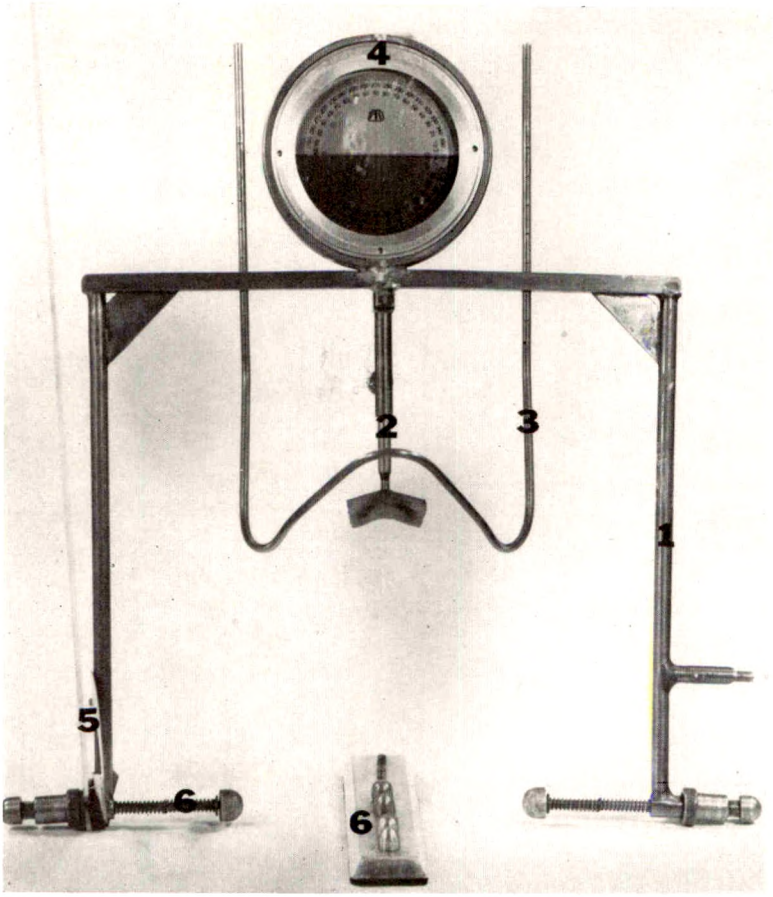


FIG. 1. The head positioning device consists of 6 parts: (1) Aluminum frame; (2) median supporting bar; (3) cheek gauge; (4) leveler; (5) angle indicator; and (6) adjustable ear plugs with coil springs.

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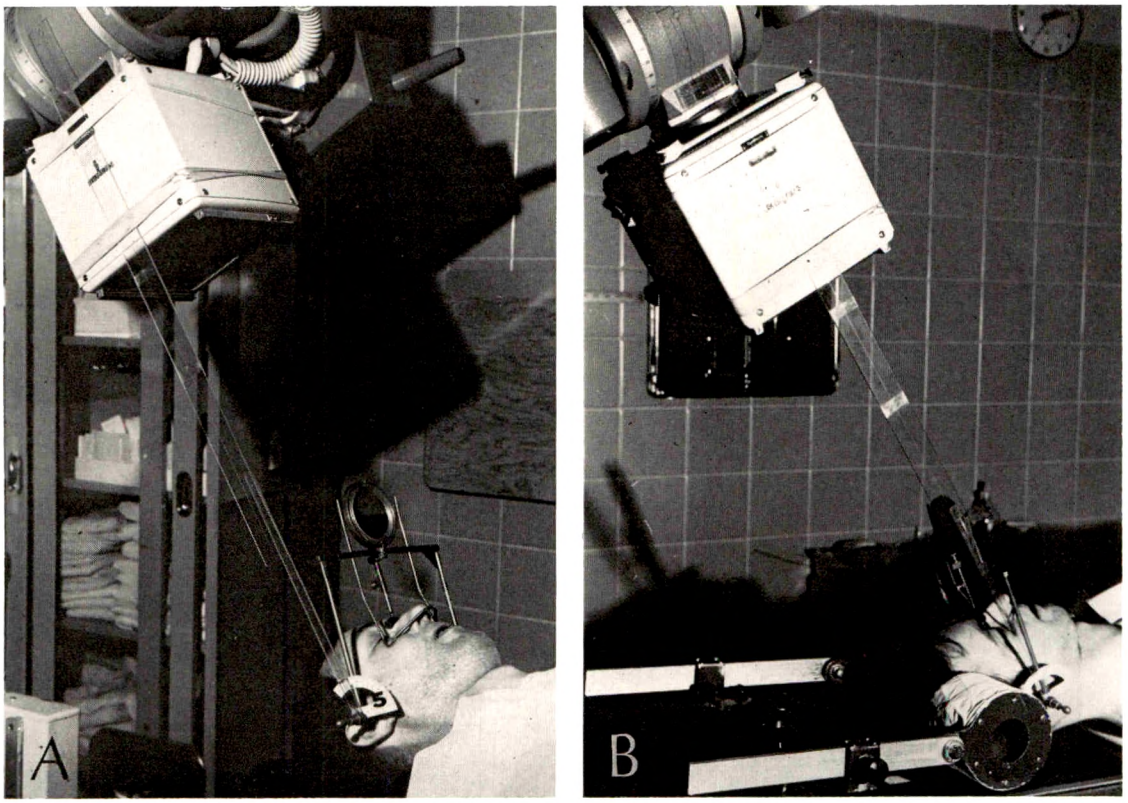


Fig. 2. (*A* and *B*) A long plastic ruler attached to the roentgen-ray cone is angled so that the angle indicator coincides with or is parallel to the plastic ruler.

clamp, a cheek gauge is used. The metal frame usually coincides with the canto-meatal line. The angle indicator is then set for a desired angulation (*e.g.*, 12° for carotid angiogram and 25° for brachial angiogram). In order to obtain a desired tube angulation, a long plastic ruler attached to the roentgen-ray cone is angled in such a way that the angle indicator coincides with or is parallel to the plastic ruler (Fig. 2, *A* and *B*).

DISCUSSION

Even a slight degree of rotation of the head (*e.g.*, 5°) in the anteroposterior projection at times may cause a distortion of anatomic structures on the angiogram or pneumoencephalogram and lead to an erroneous diagnosis.

Tilting of the head in the lateral projection may also cause false deviation of the sylvian vessels, superior sagittal sinus, internal cerebral vein, and basilar vein on the cerebral angiogram. A similar problem arises in the air study; a slight rotation or tilting of the head can give an erroneous impression of distortion or displacement of the trigones and temporal horns.

CONCLUSION

The head positioning device is extremely useful in reproducing any desired techniques if all the technical factors of the previous filming are known.

This device can be used for the positioning of the head during brain scanning, especially for follow-up studies.

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Liaison Representatives on the National Council on Radiation Protection and Measurements: Herbert M. Parker, Richland, Wash.; Marvin M. D. Williams, Rochester, Minn.

Representative on The Board of Chancellors of the American College of Radiology: Juan A. del Regato.

Fifty-second Annual Meeting: Hotel Coronado, San Diego, Calif., March 1–6, 1970.

EDITORIALS

FIFTY-FIRST ANNUAL MEETING OF THE AMERICAN RADIUM SOCIETY

THE Fifty-first Annual Meeting of the American Radium Society was held at the Bellevue-Stratford Hotel in Philadelphia on April 28, 29 and 30, 1969. Fifty-one years ago the Society was first organized in Philadelphia at the Rittenhouse Hotel for its First Annual Meeting. A second meeting was again held in the same city in 1931. The attendance by members and guests amounted to a total registration of 569, representing 156 members, 187 scientific guests, 112 ladies and 114 residents.

Dr. Juan del Regato officially called the meeting to order in the beautiful Rose Garden Room on the eighteenth floor of the Hotel. He called on Dr. Theodore H. Mendell, President of the Philadelphia County Medical Society, who welcomed the American Radium Society to Philadelphia. He pointed out how important our Society had become in its growth in membership and in its scientific development in the treatment of malignant disease from the time it organized in 1916 with 18 Charter Members.

Dr. del Regato continued the meeting with his Presidential Address titled "The Community Cancer Hospital." In the past, the mere diagnosis of cancer constituted a social threat. The products of clinical endeavors are not as dazzling as the results of brilliant laboratory research. These partial solutions demand highly specialized institutions and skills. At the turn of the century with the discovery of radium and roentgen rays, a need arose for a cooperative multidisciplinary effort with a strong implication for centralization. In 1930, the American College of Surgeons recommended the formation of Cancer Clinics in approved general hospitals. These clinics have not proved to be an ideal way of managing the problems of the cancer patient; they have notoriously failed in University Hospitals. About 20 years ago, the author was invited to organize and direct a private full-time staff cancer hospital; he responded with a part-time staff cancer hospital to work in conjunction with a general hospital with the establishment of four major functions of diagnosis, treatment, education and research. He developed what has become to be known as a community cancer hospital. This kind of organization is a fruitful possibility in almost any city of moderate size and resources.

The first scientific session followed with Dr. Fernando G. Bloedorn acting as Chairman. Dr. W. E. C. Allt of the Ontario Cancer Institute of Toronto spoke on supervoltage radiotherapy of advanced carcinoma of the cervix. The 5 year survival analysis of 57 cases treated by Co^{60} teletherapy and 61 cases treated on the betatron revealed a significant difference between the 2 groups. The first group showed a 32 per cent survival, whereas the betatron group showed a 60 per cent survival and less morbidity. Dr. J. Newall of New York, N.Y. presented his system of treatment of carcinoma of the cervix using a linear intracavitary source and external irradiation and demonstrated that his method was not only effective but was with no undue risk. Dr. M. F. Strockbine and his co-workers from Houston gave a detailed account of complications in 831 patients with carcinoma of the cervix treated with 3,000 rads or more to the whole pelvis. Dr. Ruth Guttmann of New York, N.Y. reported on a 10 year study of the significance of postoperative irradiation in carcinoma of the cervix using a 2 MV. roentgen ray unit.

Later in the morning session, reports were given on the prognostic significance of radiation-induced tumor regression in carcinoma of the uterine cervix and late second cancers of the cervix after apparently successful initial radiation therapy.

Dr. Margaret H. Sloan of the U.S. Public Health Service gave a current report on the role of the regional medical programs. She stated that the latest advances in diagnosis and treatment would be made available to patients through the medical profession and medical institutions. The planning grants of 1965 would cover 55 regional medical programs which would vary in size and population served. In the field of Radiology, regional medical programs should strive to improve the quality and availability of both diagnostic radiology and radiotherapy. Additional training programs at both the physician and technologic level are supported. Support for equipment is given only under special circumstances.

Three presentations on radiobiology were given and included temporary spontaneous regression of isologous tumor transplants in irradiated tissue, experimental observations of preoperative *versus* postoperative irradiation on an animal tumor system and a metabolic control with the use of insulin and glucose for the enhancement of radiation response.

The morning session was completed by an interesting symposium on tumors of the eye. Dr. Martha Southard acted as Chairman and the panel consisted of Dr. George Merriam, Dr. Malcolm Bagshaw and Dr. Elizabeth Focht. Dr. Merriam gave his experiences on management as well as earlier and later treatment techniques in retinoblastoma. Dr. Focht reviewed dosage levels in the production of cataract and Dr. Bagshaw reported on experiences with the linear accelerator in the treatment of retinoblastoma and metastatic tumors of the eye.

The Ladies' social program on the first day of the meeting included a sight-seeing trip around Philadelphia in the morning hours, luncheon at Philadelphia 1700, special guided tour in the afternoon of the Philadelphia Museum of Art and reception for all members and guests in the evening in the Viennese and Burgundy Rooms of the Hotel, the Radium Chemical Company acting as host.

The second scientific session began on Tuesday morning with Dr. Clifford L. Ash of Toronto acting as Chairman. He called on Dr. J. F. Bohorquez who reported on a study of 550 cases of carcinoma of the lip which he managed in Newfoundland, Canada with either external roentgen therapy or radium applications between 1945 and 1955. The next two subjects were: integrated radical radiotherapy and surgery for oral and laryngeal carcinomas, and therapeutic integration of cancer of the larynx. Dr. G. H. Fletcher and associates of Houston in a review of 276 patients with squamous cell carcinoma of the supraglottic area of the larynx treated between 1948 and 1965 gave a detailed analysis of the effectiveness of the modalities of treatment. This paper was followed by one read by one of the guest speakers from France, Dr. C. M. Lalanne of the Institut Gustave Roussy, who gave a statistical report on cobalt 60 teletherapy for carcinoma of the hypopharynx and larynx. He introduced a third classification to include the ridge separating the larynx and hypopharynx. Before the morning intermission, Dr. B. H. Feder and his co-workers reported on treatment failure and cobalt 60 dosimetry in carcinoma of the vocal cord.

Following the morning intermission, Dr. Laurance V. Foye, Jr. of the National Institutes of Health summarized the investigative work on chemotherapy which is now going on as cooperative clinical research of the National Cancer Institute. Dr. J. Dutreix from the Institut Gustave Roussy reported on regression of tumors of the tonsils following different regimens of fractionation. Dr. V. A. Marcial of Puerto Rico gave a prospective study on dose fractionation on carcinoma of the base of the tongue comparing uninterrupted and split-course irradiation techniques.

The highlight of the meeting was the presentation of the Janeway Lecture. After an eloquent introduction by Dr. del Regato, Dr. Franz Buschke spoke on the subject "Radiation Therapy: The Past, The Present and The Future." He reviewed the history of radiation therapy in 4 rather distinct periods.

The first period started soon after the discoveries of radium and x rays and lasted until the early 1920s. Most of the treatment was essentially local radium, was done by surgeons and was heavily influenced by workers at Memorial Hospital, New York. Dr. Henry Janeway, a surgeon, together with Dr. Failla was instrumental in developing methods of interstitial irradiation which represented the massive single dose type of therapy. This approach represented treatment resulting in slough and necrosis. The aim was to deliver the highest possible dose in the shortest possible time.

The second period was influenced mainly by the French school of the Institut Curie and by the Radiumhemmet. The basic philosophy was to cause selective destruction of the tumor with as little damage as possible to the surrounding structures. This approach still remains one of the most important means in the art of good radiation therapy. Radiobiologic research reached a milestone with the classic investigation of the mechanism of radiation sterilization of the ram's testicle by Claud Regaud in 1919. Coutard applied the principle of divided doses given in longer periods of time to the treatment of epitheliomas. The real importance of Coutard's approach was the meticulous daily examination of the patient to observe the effects of irradiation on the tumor and surrounding normal tissues.

The third phase of development of radiotherapy placed emphasis on accurate treatment planning, based on detailed physical accuracy and dosimetry, developed by the British schools. A close cooperation between radiotherapist and physicist was required in the planning of the individual course of therapy. The "dosimetrist" was created as a new member of the team. Institutions with an adequate staff of physicists and dosimetrists working in concert with the radiotherapists and using equipment of higher voltages became the desiderata in the daily routine.

The fourth period of development, which brings us to the present, embraces the general philosophy which has taken shape during the last 20 to 30 years. The emphasis on sound, statistical proof required the introduction of rigid protocols which were at times followed despite the clinical necessity of modification for individual patients. Much progress has been made during the last four decades, the most important of which is our ability to avoid significant radiation damage to the vasculoconnective tissue. Technically correct radiation therapy today is safe.

Dr. Buschke closed his address by stating that certain pitfalls should be avoided. (1) Radiation therapy should not be spread out into too many small hospitals, but it should be centralized in large institutions which are adequately equipped and which provide a competent staff of specialists in other fields who will make up an oncologic unit. (2) Although the physical accuracy of dose delivery has markedly improved during the last decade, we should not forget that the physician has so far not been replaced in the treatment of cancer. (3) Uniformity and rigid programs should be avoided; adjustment to local situations and personalities should be made.

The Ladies' program in the morning included a bus trip to Winterthur, with a tour of the gardens, colonial rooms and museum.

The Atomic Energy of Canada, Ltd. was host to a reception in the early evening hours in the Terrace and South Cameo Rooms. The Annual Banquet followed in the Rose Garden on the eighteenth floor. Dr. Juan del Regato introduced the distinguished personalities at the speakers' table and in the audience. He presented the Certificate of Recognition to Dr. John L. Pool, the immediate past president. Following a detailed account of Norse mythology, Dr. del Regato with appropriate cere-

mony presented the Janeway Medal to Dr. Franz Buschke in recognition of his valuable contributions in the treatment of cancer. Members and guests also participated in dancing during the evening.

Dr. H. Peter Mueller acting as Chairman opened the third scientific session on Wednesday morning with a discussion of pseudolymphomas by Dr. R. Robbins and patterns of progression and factors influencing recurrence of malignant lymphomas by Dr. D. W. Molander.

Three interesting presentations on tumors in children followed later in the program. Dr. J. G. Stella and his co-workers reported on the management and results of 144 cases of neuroblastoma treated in the Institut Gustave Roussy over a period of 7 years. Dr. R. H. Sagerman and associates reviewed the evolution of a treatment program of Wilms' tumor. Dr. Melvin Tefft and co-workers reported on early and late effects of irradiation of the liver in the treatment of Wilms' tumor or neuroblastoma. Dr. J. M. Vaeth quoted Deuteronomy 23 when he gave an account of his experiences of treating 6 cases of carcinoma of the penis in the past $3\frac{1}{2}$ years with external irradiation using short distance cesium therapy.

Following the morning intermission, a variety of subjects was presented including chemotherapy of malignant tumors, host resistance and survival in medullary cancer of the breast, radiotherapy in the management of sarcomas of the soft tissues, treatment of metastatic cervical lymph nodes by radiation alone and the management of the teeth, bone and soft tissues in patients receiving treatment for oral cancer. The last 2 papers of the meeting dealt with moving strip techniques. Dr. F. Mincer and co-workers presented an interesting report on moving strip irradiation in the treatment of extensive neoplastic disease in the chest and Dr. A. B. Friedmann and co-workers spoke on total abdominal Co^{60} irradiation by moving strip therapy.

The Fifty-first Annual Meeting of the American Radium Society proved to be most interesting from the standpoint of an excellent scientific program and by the unusual cultural attractions of the Philadelphia area. The members and guests of the Society are indebted to its President, Dr. Juan del Regato for his splendid endeavor in developing an interesting scientific program, to Dr. Luther W. Brady and the members of the Arrangements Committee, and to the Management of the Bellevue-Stratford Hotel, for their efforts in providing many excellent facilities.

Harry Hauser, M.D.

3395 Scranton Road
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DANIEL THOMAS QUIGLEY, M.D.
1876–1968

DANIEL Thomas Quigley was born at Baraboo, Wisconsin in 1876 and graduated from Rush Medical College, M.D. in 1902. He interned at the Englewood Hospital and served an apprenticeship under the famous surgeon, Dr. J. B. Murphy. Thereafter, he practiced in North Platte, Nebraska where he organized the first public health officers association. He was a founder of the American College of Surgeons. In 1913–1914 he did postgraduate study in London, Vienna and in Paris where he knew the Curies. He returned with 100 mg. of radium, which was the first radium placed in clinical service west of New York City.

In 1916 he participated in the founding of the American Radium Society. He moved to Omaha in 1917 where he opened the thirty bed Radium Hospital. He became a member of the Faculty at the University of Nebraska College of Medicine

where he served in Surgical Pathology and was in charge of radium therapy until 1931.

He was the author of several publications, perhaps the best known being "The Conquest of Cancer" published in 1929—a well illustrated documentary on the effects of radiation. Later he became quite interested in dietary factors as related to cancer.

Dr. Quigley continued in the practice of radiotherapy at his office in the Omaha Medical Arts Building until 1966, retiring at the age of 90 due to generalized arteriosclerosis.

His range of interests was very wide. He was a pioneer in aviation being on the Committee that picked the site of the present Omaha Air Port. He had a host of important friends with whom he corresponded, including among others Henry L. Menken, William Osler, Harvey Cushing and Clarence Darrow.

He died on October 2, 1968 after a prolonged illness and is survived by his son, Thomas B. Quigley, M.D., Clinical Professor of Surgery at Harvard Medical School.

Dr. Quigley was the last surviving Charter Member of the American Radium Society.

Howard B. Hunt, M.D.

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NEWS ITEMS

AMERICAN RADIUM SOCIETY ELECTS OFFICERS

At the Fifty-first Annual Meeting of the American Radium Society held at the Bellevue Stratford Hotel, Philadelphia, Pennsylvania, April 27–30, 1969, the following officers were elected: *President*, Dr. Fernando G. Bloedorn, Boston, Massachusetts; *President-Elect*, Dr. James F. Nolan, Los Angeles, California; *1st Vice-President*, Dr. Arthur I. Holleb, Houston, Texas; *2nd Vice-President*, Dr. M. Vera Peters, Toronto, Ontario, Canada; *Secretary*, Dr. John V. Blady, The Parkway House, 2201 Benjamin Franklin Parkway, Philadelphia, Pennsylvania 19130; *Treasurer*, Dr. Antolin Raventos, 3400 Spruce Street, Philadelphia, Pennsylvania 19104.

The *Chairman of the Executive Committee* is Dr. Milton Friedman, New York, New York.

The Fifty-second Annual Meeting of the Society will be held in San Diego, California, March 1–6, 1970.

NATIONAL BUREAU OF STANDARDS (NBS)

Temporary Suspension of X-Ray Calibration Services

The Dosimetry Section of the National Bureau of Standards is suspending temporarily the calibration of roentgen meters for moderately- and heavily-filtered x rays. These categories are identified as all MF and HF techniques in the schedule of tests given in NBS *Miscellaneous Publications* 250. Calibrations for other qualities will be performed as usual, as will calibrations for cesium 137 and cobalt 60 gamma rays. The suspension of services for the M and H techniques will allow the Section to reduce a large backlog of calibration work and provide time for installation of automatic equipment.

It is anticipated that these services will again be provided in the latter part of 1969 at which time an announcement will be made. A list is being maintained of those who request calibrations and they will be notified, in the order in which the requests are received, when to submit their roentgen meters for calibration.

Some capability for calibrations in the M and H categories will be maintained and exceptions to the suspension will be made in special cases where a delay in calibration will impose a severe hardship.

SOCIEDAD ARGENTINA DE RADIOLOGÍA

At the recent meeting of the Sociedad Argentina de Radiología the following officers were elected for 1969–1970: *Presidente*: Dr. Eduardo A. Navarrine; *Vice-Presidente*: Dr. Jorge E. Barragué; *Secretario General*: Dr. Juan R. Heilbuth Pacheco; *Secretario de Actas de Radiodiagnóstico*: Dr. Armando De Onaindia; *Secretario de Actas de Radioterapia*: Dr. Oriel Alva; *Tesorero*: Dr. Thomas J. Gutierrez; *Vocales*: Dr. Marcelo O. Sanromá and Dr. Carlos F. Lanari; *Director de la Revista*: Dr. Marcelo H. Moreau.

The address of the Secretary-General is Sante Fe 1171, Buenos Aires, Argentina.

SYMPOSIUM OF THE DIAGNOSTIC RADIOLOGY OF GASTROINTESTINAL BLEEDING

On October 31 and November 1, 1969, the Department of Diagnostic Radiology of the Lahey Clinic Foundation will sponsor a "Symposium on the Diagnostic Radiology of Gastrointestinal Bleeding."

The faculty of the Symposium will consist of members of the Staff of the Lahey Clinic Foundation and invited guest speakers.

Inquiries for additional information should be directed to: Robert E. Wise, M.D., Chairman, Department of Diagnostic Radiology, Lahey Clinic Foundation,

605 Commonwealth Avenue, Boston, Massachusetts 02215.

CONFERENCE IN NUCLEAR MEDICINE

Halifax, Nova Scotia, Canada

A Conference in Nuclear Medicine sponsored by the Department of Therapeutic Radiology and Nuclear Medicine of the Victoria General Hospital and the Department of Continuing Medical Education of Dalhousie Medical School in Halifax, Nova Scotia, will be held on September 5 and 6, 1969.

Included among those invited are: Dr. H. N. Wagner of Johns Hopkins Hospital, Baltimore; Dr. E. James Potchen of Washington University, St. Louis; Dr. L. Rosenthall of Montreal; and Dr. D. Wood of Toronto General Hospital.

Further information may be obtained from the Director, Department of Continuing Medical Education, Dalhousie University Medical School, Halifax, Nova Scotia.

UNIVERSITY OF CAMBRIDGE SCHOOL OF CLINICAL RESEARCH AND POSTGRADUATE MEDICAL TEACHING

Medical Isotope Course

A co-ordinated course will be held from September 22 to October 24, 1969, involving periods of study at the Atomic Energy Research Establishment, Harwell, at the Cambridge Postgraduate Medical School, and in London at the Middlesex Hospital Institute of Nuclear Medicine, the Royal Postgraduate Medical School and M.R.C. Cyclotron Unit, and the Royal Marsden Hospital and Institute of Cancer Research.

The course has been organized by Professor J. S. Mitchell in collaboration with Dr. E. W. Emery, Mr. R. A. Faires, Dr. V. R. McCready, Dr. N. G. Trott, Mr. N. Veall and Dr. E. S. Williams.

Two weeks, September 22 to October 3, will be spent at Harwell as a preliminary to the Cambridge and London courses and will provide an introduction to handling and measuring radioactive materials, mainly at the tracer level.

Two weeks, October 6 to 17, will be spent at the Cambridge Postgraduate Medical School Department of Radiotherapeutics and will include lectures and demonstrations with opportunities for practical work in experiments on the medical uses of radioisotopes.

In the fifth week, October 20 to 24, students will divide their time between the three institutions and hospitals in London and at each of these a particular group of topics will be covered.

Details concerning registration and program can be obtained from the Secretary, Cambridge University Medical School, Hills Road, Cambridge CB2 1QT.

HEALTH PHYSICS SOCIETY

Mid-year Symposium on Electronic Product Radiation and the Health Physicist

The recent Radiation Control for Health and Safety Act (PL 90–602) has placed increased demands on the Health Physicists, Industrial Hygienists and others in positions responsible for personnel safety. This legislation providing for control of both ionizing and non-ionizing electronic produced radiation necessitates that all safety personnel become more aware of potential hazards associated with such equipment; *i.e.*, lasers, microwave generating equipment, diathermy apparatus, x-ray producing devices, particle accelerators, etc.

A symposium covering these subjects — the 4th Annual National Health Physics Society Midyear Topical Symposium, sponsored by the Blue Grass Chapter of the Health Physics Society—will be conducted at the Brown Hotel, Louisville, Kentucky, January 28–30, 1970.

The meeting will be devoted to practical problems concerning basic engineering design, dosimetry and calibration techniques, associated biologic hazards, threshold injury

values and regulatory safety measures.

The program will include invited papers and contributed papers. Abstracts not exceeding 200 words should be submitted to the Symposium Chairman by October 1, 1969.

All persons with an interest in these topics are invited to participate.

For additional information regarding the program and exhibits, please contact the Symposium Chairman, Dr. Wordie H. Parr, US Army Medical Research Laboratory, Fort Knox, Kentucky 40121.

AMERICAN ASSOCIATION OF PHYSICISTS IN MEDICINE

Mid-Atlantic Chapter

The 1970 mid-year meeting of the American Association of Physicists in Medicine will be held at the Park-Sheraton Hotel, Washington, D. C., July 13–15, 1970.

The theme of this meeting will be "Current Topics in Medical Physics."

Inquires should be addressed to: Major James A. Hancock, Jr., Box 2546 Malcolm Grow USAF Hospital, Andrews Air Force Base, Washington, D. C. 20331.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

Chronic Ulcerative Colitis: A Lifelong Study. By J. Arnold Bargen, M.D., Clinical Professor of Medicine, University of California at Irvine; Consultant in Gastroenterology, Riverside Medical Clinic, Riverside, Calif.; Emeritus Professor of Medicine, Mayo Graduate School of Medicine; Former Chairman, Department of Gastroenterology, The Mayo Clinic, Rochester, Minn.; Senior Consultant in Gastroenterology, Scott and White Clinic; Director of Medical Education, Scott and White Memorial Hospital and Scott, Sherwood and Brindley Foundation, Temple, Texas. Cloth. Pp. 123, with many illustrations. Price, $7.50. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62703, 1969.

In a 6×9 inch book of 123 pages the author reviews his 44 years of experience with more than 5,000 of his own patients who had chronic ulcerative colitis.

The book is not a reference or textbook but is an easily readable, "down to earth" presentation of the author's clinical approach to the diagnosis and treatment of ulcerative disease of the colon.

Problems with diagnosis, treatment and complications are discussed and amplified by means of 19 case reports. A clinical classification: insidious, severe and fulminating, is used as the framework for discussions on common chronic ulcerative colitis with the less common forms listed as regional colitis, ileocolitis and colitis due to a specific causative agent. This simplified classification avoids most argument, but it should be remembered that Dr. Bargen is a super-expert in the field, has published more than 138 papers concerning colon diseases, and in this small book he is attempting to give the benefits of his life-time learning to the non-expert.

The book should be of great value to the general practitioner and internist who do not have a great deal of knowledge or experience with non-malignant disease of the colon.

Clyde A. Stevenson, M.D.

Fundamental Problems in Scanning. Compiled and Edited by Alexander Gottschalk, M.D., Associate Professor of Radiology, Director of the Argonne Cancer Research Hospital, Director of Section of Nuclear Medicine, Department of Radiology, University of Chicago; and Robert N. Beck, B.S., Associate Professor of Radiological Sciences, Department of Radiology and Argonne Cancer Research Hospital, University of Chicago, Chicago, Illinois. Cloth. Price, $26.95. Pp. 410, with many illustrations. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62703, 1968.

This text represents an outgrowth of a most unique symposium from the Argonne Cancer Research Hospital in 1965 under the sponsorship of Abbott Laboratories, the Northwestern University School of Medicine, and the Argonne Cancer Research Hospital. Until this time the number of symposia on nuclear medicine that had been presented were primarily concerned with the art of clinical scanning, interpretation and laboratory techniques. This symposium was conceived to examine the entire radioisotopic imaging process and to fill the gap between problems of obvious clinical interest and those concerning techniques of instrumentation.

Many of the contributors to this text were asked to discuss theoretic concepts which had not been studied in the past; therefore, in some respects, representing "works in progress." Manuscripts are included in the text that were not presented at the symposium; some representing an enlargement of ideas presented in the excellent discussions, and others that are entirely new in order to keep the volume up to date in this rapidly expanding diagnostic modality.

This text is a compendium of most of the areas of instrumentation in nuclear medicine; yet the design encompasses techniques that may be used in the future and points out promising technical leads. The editors have enlisted the expertise of 38 of the major contributors in the field of imaging, perception, and in-

strumentation. To present in a single volume the varied subjects is a monumental task; the editors have realized admirably their objectives in providing a reference text for those individuals concerned with the instrumentation problems of radioisotope imaging.

The contents are organized into 5 sections in an attempt to categorize the many concepts. However, the reader is still forced to oscillate between many topics. The section on "Collimation and Detection Modes" is particularly good and the chapters on "Sensitivity and Resolution of the Scintillation Camera" and "Applicability of Vacuum Image Intensification Chains to Radioisotope Imaging" are superior. Although this same information might be gleaned from a search of texts and journals regarding these subjects, it is here consolidated in a concise, well edited form.

To make the discussions informative and to the point, an informal colloquium was arranged for the faculty the day preceding the symposium. This arrangement enhanced the success of the discussion. If any criticism of the text is to be made by this reviewer, it would be leveled at the short chapters that serve as communications to provide information on new and untested imaging techniques. Although somewhat distracting, these chapters probably attest to the change and rapid growth of the field of instrumentation in nuclear medicine.

In summary, "Fundamental Problems in Scanning" is not aimed at the individual with a casual interest in nuclear medicine. It is a sophisticated, occasionally mathematical, reference text addressed to the worker in the field of scanning and provides him with unique information regarding instrumentation problems. In this framework it is an extremely interesting and useful book.

A. Everette James, Jr., M.D.

BOOKS RECEIVED

Lung Calcifications in X-Ray Diagnosis. By Emanuel Salzman, A.B., M.D., F.A.C.R., Director of Radiology, Denver General Hospital; Associate Clinical Professor of Radiology, University of Colorado School of Medicine; Consultant in Radiology, Denver Veterans Administration Hospital, Denver, Colorado. Cloth. Pp. 123, with many illustrations. Price, $7.50. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62703, 1968.

Cell Cultures for Virus Vaccine Production. National Cancer Institute Monograph 29, December, 1968. Conference on cell cultures for virus vaccine production; held November 6–8, 1967, Clinical Center, National Institutes of Health, Bethesda, Md. Sponsored by Division of Biological Standards, National Institutes of Health, Bethesda. Conference Chairman and Editor, Donald J. Merchant. Cloth. Pp. 608, with some figures. Price, $7.25. Superintendent of Documents, U. S. Government Printing Office, Washington, D. C. 20402, 1968.

Angiography of Cerebral Circulation. By Kurt Decker and Herbert Backmund, Munich. Cloth. Pp. 76, with 148 illustrations. Price, $12.00. Georg Thieme Verlag, Stuttgart. In the USA and Canada, Intercontinental Medical Book Corporation, New York, N. Y. 10016, 1969.

Radiologic Clinics of North America. Symposium on Radiology of the Alimentary Tract. Guest Editor, Richard H. Marshak, M.D. Volume VII, No. 1, April, 1969. Cloth. Pp. 191, with many illustrations. W. B. Saunders Company, West Washington Square, Philadelphia, Pa. 19105, 1969.

Paramedical Dictionary: A Practical Dictionary for the Semi-medical and Ancillary Medical Professions. By J. E. Schmidt, M.D. Cloth. Pp. 423. Price, $8.75. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62703, 1969.

A Radiographic Standard of Reference for the Growing Knee. By S. Idell Pyle, Ph.D., Department of Anatomy, Case Western Reserve University School of Medicine, Cleveland, Ohio; and Norman L. Hoerr, Ph.D., M.D. Cloth. Pp. 135, with many illustrations. Price, $6.25. Charles C Thomas, Publisher, 301–307 East Lawrence Avenue, Springfield, Ill. 62703, 1969.

Collateral Circulation in Clinical Surgery. Edited by D. E. Strandness, Jr., M.D., Chief, Peripheral Vascular Service, Veterans Administration Hospital, Seattle; Associate Professor of Surgery, University of Washington, School of Medicine, Seattle. Cloth. Pp. 633, with 242 illustrations. Price, $18.50, U.S.; $20.00, Canada. W. B. Saunders Company, West Washington Square, Philadelphia, Pa. 19105, 1969.

Lung Cancer: A Study of Five Thousand Memorial Hospital Cases. Edited by William L. Watson, M.D., Emeritus Chief, Thoracic Service, and Attending Surgeon, Special Surgical Service, Memorial Hospital for Cancer and Allied Diseases; Emeritus Surgeon Director and Consulting General Surgeon, Manhattan Eye, Ear, and Throat Hospital; Emeritus Clinical Associate Professor, Cornell University Medical College. Cloth. Pp. 584, with 454 illustrations. Price, $29.50. C. V. Mosby Company, Publishers, 3207 Washington Boulevard, St. Louis, Mo. 63103, 1969.

Information Transmission in Roentgen Diagnostic Chains: Experimental and Clinical Studies. By Erkki M. Laasonen. Acta Radiologica Supplementum 280. Paper. Pp. 193, with many figures. Price, Sw. Kr. 35:-. Acta Radiologica, Stockholm 2, Sweden, 1968.

Arthrography of the Knee Joint in Children: Roentgenologic Anatomy, Diagnosis and the Use of Multiple Discriminant Analysis. By Rasmus Stenström. Acta Radiologica Supplementum 281. Paper. Pp. 86, with some figures. Price, Sw. Kr. 35:-. Acta Radiologica, Stockholm 2, Sweden, 1968.

Carcinoma of the Uterine Corpus: Factors Bearing on the Curability. By Karl Karlstedt. Acta Radiologica Supplementum 282. Paper. Pp. 98, with some figures. Price, Sw. Kr. 35:-. Acta Radiologica, Stockholm 2, Sweden, 1968.

Pharmacodynamic Response of Epidermal Hyperplasias to Topical Vinblastine Treatment: an Electron Microscopic Study in Mice. By Leo Stjernvall. Acta Radiologica Supplementum 283. Paper. Pp. 120, with some figures. Price, Sw. Kr. 35:-. Acta Radiologica, Stockholm 2, Sweden, 1968.

Distribution and Kinetics of Labelled Vitamin B_{12}. By Hans Flodh. Acta Radiologica Supplementum 284. Paper. Pp. 80, with many illustrations. Price, Sw. Kr. 35:-. Acta Radiologica, Stockholm 2, Sweden, 1968.

Progress Against Cancer, 1969. A Report by the National Advisory Cancer Council. U. S. Department of Health, Education, and Welfare. Paper. Pp. 83, with many illustrations. Price, $1.50. Superintendent of Documents, U. S. Government Printing Office, Washington, D. C. 20402, 1969.

Angiographie und ihre Leistungen: Technik, Ergebnisse, Fortschritte. By Kurt Egon Loose. Paper. Pp. 270, with 245 figures. Price, DM 59.–. Georg Thieme Verlag, Stuttgart. In the USA and Canada, Intercontinental Medical Book Corporation, New York, N. Y. 10016, 1968.

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ROENTGEN DIAGNOSIS

Head

Stevenson, G. W., and Gossman, H. H. Dental and intracranial actinomycosis. *Brit. J. Surg.*, Nov. 1968, *55*, 830–834. (Address: Dr. G. W. Stevenson, Registrar, Department of Diagnostic Radiology, Leeds General Infirmary, Leeds, England.)

Actinomycetaceae are common residents in the normal human mouth.

The authors report the occurrence of an intracranial abscess in a 50 year old male admitted to the hospital following an attack of motor Jacksonian epilepsy. On admission, the patient was found to be diabetic, but there was no evidence of pyogenic infection in either the peripheral blood or cerebrospinal fluid. Because of progressive drowsiness and left hemiparesis, right carotid angiography was performed and revealed an avascular mass in the posterior frontal region depressing the sylvian triangle. Aspiration of the mass yielded 50 ml. of thick pus. Bacteriologic investigation established the causative organism as an *Actinomycetes*. Sterile colloidal barium was introduced into the abscess cavity, and serial roentgenograms were employed to follow the course of the lesion over the next 9 months. On appropriate chemotherapy, there was a gradual clinical improvement with reduction in the size of the contrast collection.

The authors comment that the organism probably reaches the central nervous system by the blood stream. The patient was found to have an abscessed mandibular incisor tooth which was extracted. They state that the avascularity of an actinomycotic abscess, poorly penetrated by systemic antibiotics, makes surgical drainage, or, if feasible, complete excision of the lesion essential.—*Stephen A. Kieffer, M.D.*

Wright, J. T., and Benjamin, Bruce. Cycloidal tomography of the temporal bone. *Australasian Radiol.*, Nov., 1968, *12*, 320–327. (From: The Department of Radiology, Sydney Hospital, Sydney, N.S.W., Australia.)

In the past the temporal bone has been examined by ordinary roentgenograms. Many special views have been advocated for examination of this bone, and this multiplicity of views testifies to the unsatisfactory state of these methods of examination. The main difficulty is that the important structures of the middle and inner ear are very small and surrounded by dense bone.

Tomography is the obvious way to get around this difficulty, but linear tomography has been unsatisfactory in that it produced obscuring linear streaks on the film. Cycloidal tomography has removed this difficulty since the tube can travel much further in a circle without undue angulation of the beam, giving a thinner cut, and the blurred structures are spread over a wider area, becoming less obtrusive. The attic walls can be clearly defined, and the body of the incus and the head of the malleus can also be distinguished. Other structures which can be clearly defined in other cuts are the cochlea, the vestibule with the oval window niche, and the semicircular canals.

The authors state that cycloidal tomography is the best way of investigating the internal auditory canal. In comparison with the old series of views of the internal canal, tomography was found to be easier and required fewer films, so that it has replaced all other methods.

In facial nerve paralysis following head injury, usually associated with severe vertigo and deafness, tomographic cuts can show the site of the fracture. In tumors of the external and middle ear the presence and extent of bone erosion can be assessed. Another important contribution of this technique is in the field of congenital atresia, where it is important to define the presence or absence of the external auditory canal, the ossicles and the middle ear cavity, and the normality of the cochlea and internal auditory canals.—*Douglas S. Kellogg, M.D.*

Wortzman, G., Barnett, H. J. M., and Lougheed, W. M. Bilateral internal carotid occlusion: a clinical and radiological study. *Canad. M. A. J.*, Dec. 21, 1968, *99*, 1186–1196. (From: The Department of Radiology, Toronto General Hospital, 101 College Street, Toronto 2, Ontario, Canada.)

Fifty per cent of the patients with cerebrovascular insufficiency have extracranial occlusive vascular disease, and in up to 74 per cent there are multiple lesions.

The commonest sites of stenotic lesions are at the origins of the vertebral and internal carotid arteries, and if one carotid sinus shows severe stenosis, there is only a 19 per cent chance that the other carotid sinus will be normal.

Following surgical repair of the stenotic extracranial lesion, there is a restoration flow in occlusive carotid disease in 25 per cent of cases when operation is no more than 4 days after the occlusion. The percentage increases to 66 per cent when early operation can be carried out.

Bilateral internal carotid occlusion is not a common finding and the authors have encountered only 17 cases since 1959 in their investigations of cerebrovascular disease.

In this series the average age of the patients was 53 years, with a sex incidence of 13 males to 4 females, and an earlier age of onset in male patients. Nine of the 17 patients never did have a history or physical findings to indicate bilateral disease, but in the other 8, 2 had a history of stroke on the opposite side pre-

vious to their present episode. The remaining 6 had recognizable evidence of bilateral disease, but the clinical evidence was predominantly unilateral in 3.

Impairment of intellectual function of sufficient severity to justify the term dementia occurred in 10 of these cases, while 2 others had definite intellectual decline of lesser degree.

The outcome for the patients in this series was poor, with 5 immediate deaths and another died 5 years later in a mental hospital. Six had major residual disability and only 4 were able to return to useful employment. Effective operative treatment with restoration of flow was accomplished only once in the 9 patients who came to operation.

At the present time, it is widely agreed that with refinements in angiographic techniques and the use of sensible precaution, there is very little increased risk to the atherosclerotic patient and that angiography is essential both for the diagnosis and the possible correction of the atherosclerotic lesion.

The authors' cases were investigated by either 3 or 4 vessel angiography, the method being dependent on the presenting signs and symptoms, state of peripheral vessels and findings on the initial angiogram.

Selective angiography from the aortic arch was rarely carried out because of the opinion that use of increased amounts of contrast material which were necessary for that method, and the possibility of dislodged emboli from the catheter, were factors in producing increased patient morbidity.

In most cases a percutaneous right brachial puncture with retrograde injection using a pump injector, allowed visualization of the right carotid-vertebral-basilar system. In addition, the percutaneous left carotid injection was done using a Sheldon cannula, which decreases the incidence of subintimal injection. In many cases the left vertebral artery was not visualized, as operation of a stenotic vertebral lesion was not contemplated in the presence of bilateral carotid occlusion.

The authors feel that with this relatively complete angiography, patterns of collateral circulation can be traced. Interesting examples of subclavian and external carotid steal mechanisms are described as well as 2 cases of a rete mirabile variation in developed collateral blood flow. There was no exact correlation between the degree of disability and the roentgenologic findings.

In view of the poor prognosis for the patient with bilateral occlusive lesion, the authors believe that early diagnosis and surgical correction of the unilateral lesions are indicated.—*James R. Knapp, M.D.*

Neck and Chest

Baum, Gerald L., Donnerberg, Roy L., Stewart, David, Mulligan, Wallace J., and Putnam, Louis R. Pulmonary sporotrichosis. *New England J. Med.*, Feb. 20, 1969, *280*, 410–413. (From: The Ohio Tuberculosis Hospital, Columbus; the Pulmonary Section, Veterans Administration Hospital, and the Department of Medicine, Case Western Reserve University School of Medicine, Cleveland; the Pulmonary Disease Section, Veterans Administration Hospital, Cincinnati; and the Department of Medicine, University of Cincinnati, College of Medicine, Cincinnati, Ohio.)

Skin lesions are the most commonly recognized manifestation of human sporotrichosis. It is an occupational disease of professional florists, produce handlers, and gardeners. Since the *Sporotrichum schenckii* mold spores are only 2 to 3 microns in diameter, the possibility of primary pulmonary infection must be recognized. Few cases have been documented.

Roentgen findings include irregular pulmonary infiltrations, linear densities, and cavitations. They may mimic the findings in tuberculosis and histoplasmosis. While skin lesions are treated with iodides, pulmonary lesions must be treated with amphotericin B.

Diagnosis is difficult for the pathologist as well as the radiologist unless there is a high index of suspicion and a good occupational history. The organism is difficult to find in biopsied tissues, and is best seen on culture.—*Arch H. Hall, M.D.*

Leeming, B. W. A. Radiological aspects of the pulmonary complications resulting from intermittent positive pressure ventilation (I.P.P.V.). *Australasian Radiol.*, Nov., 1968, *12*, 361–377. (From: The X-Ray Department, Auckland Hospital, Auckland, New Zealand.)

In intermittent positive pressure ventilation, successive tidal volumes are applied to the lungs of the recipient by an external source of pressure which is higher than atmospheric. This external source is usually a mechanical respirator. However, the Ambu bag and mouth-to-mouth resuscitation are also forms of intermittent positive pressure ventilation.

A review of the 267 patients admitted to the Auckland Hospital Respiratory Unit during the year 1967 shows that 69 in all had roentgenologic changes indicating pulmonary edema at some time during their stay. If there is increased airways resistance, such as is found in asthma or bronchial disease, the ventilation pressure has to be further raised if it becomes necessary to maintain the tidal volume. This may lead to simple but generalized overdistention of the alveoli (simple air trapping) because of the increased airway obstruction during expiration. Excess fluid may present as a problem if the bronchial mucosa becomes edematous. Another serious complication is

that of obliterative pneumonitis (respirator lung syndrome).

Of the 267 admissions during 1967, it was found that 5 developed pulmonary interstitial emphysema, 4 during intermittent positive pressure ventilation therapy. Two died. Sixty-nine cases (26 per cent) developed pulmonary edema, and in 15 cases there seemed no adequate explanation for the edema other than factors associated with the use of a respirator. The number of cases of pulmonary edema closely related to the use of intermittent positive pressure ventilation is considered to be higher than 15, however.

Several case histories are presented, as well as reproductions of roentgenograms and photomicrographs.—*Douglas S. Kellogg, M.D.*

Fuchs, G., Friedrich-Breuninger, Gisela, and Sperling, Gisela. Klinische und röntgenologische Erfahrungen bei frühkindlicher interstitieller Pneumonie. (Clinical and roentgenologic experience in juvenile interstitial pneumonia.) *Röntgen Blätter*, Dec., 1968, *12*, 594–600. (Address: Dr. Georg Fuchs, Univ.-Kinderklinik, 87 Würzburg, Germany.)

The authors report 417 cases of interstitial pneumonia occurring in hospitalized premature infants or neonatally sick children. This infection is associated with a high incidence of pneumocystis carinii.

On microscopic examination, the bronchioles contain lymphocytes and plasma cells, are edematous, and the alveoli become progressively atelectatic. The three stages of edema, atelectasis and emphysema, may co-exist, merge with or progress from one to the other, or healing may take place at any stage.

The roentgenologic appearance is one of streaky densities radiating from the hilar regions, and varying degrees of stippling, especially in the parahilar zones. In 93 per cent, the changes are bilateral and symmetric with a butterfly pattern, miliary stippling, emphysematous alterations and hazy diaphragmatic contours. In more severe cases, the shadows are poorly delineated and confluent. The hilar lymph nodes are not involved.

The clinical signs are dyspnea, tachypnea, circumoral cyanosis, and inability to thrive. The infection usually subsides in 2–4 weeks but a few children die of pulmonary complications.

In this series, 11 patients had a pneumothorax (with an associated mediastinal emphysema in 7); 4 cases had an isolated mediastinal emphysema; 1 child developed a lung abscess.

The treatment includes oxygen, chemotherapy, antibiotics and antimycotics.—*J. Zausner, M.D.*

DeVita, Vincent T., Emmer, Michael, Levine, Arthur, Jacobs, Bruce, and Berard, Costan. Pneumocystic carinii pneumonia: successful diagnosis and treatment of two patients with associated malignant process. *New England J. Med.*, Feb. 6, 1969, *280*, 287–291. (Address: Dr. V. T. DeVita, Medicine Branch, National Cancer Institute, 12N228, Bethesda, Md. 20014.)

Pneumocystis carinii pneumonia is an uncommon disorder that occurs primarily in 1 of 4 clinical settings: in debilitated premature infants; sometimes in epidemic form; in children with hypogammaglobulinemia; and in patients given immunosuppressive agents after organ transplantations. The first has been reported primarily from Eastern Europe; the other 3 have been repeatedly observed in the United States. The disease has been uniformly fatal in adults with malignant processes.

Two case histories are presented. These patients had underlying lymphoreticular malignant disease. They were successfully treated for documented pneumocystis carinii pneumonia with pentamidine isethionate. The infection with P. carinii in an adult causes a febrile illness with a roentgenographic pattern of diffuse interstitial pneumonia. In the proper clinical setting the diagnosis should be confirmed by percutaneous needle biopsy, and adequate therapy given.

Further experience with pentamidine isethionate in histologically documented cases will permit a valid assessment of its therapeutic efficacy. One should anticipate its potential renal toxicity.— *Mary Ann Cortese, M.D.*

Hirsh, J., Hale, G. S., McDonald, I. G., McCarthy, R. A., and Pitt, A. Streptokinase therapy in acute major pulmonary embolism: effectiveness and problems. *Brit. M. J.*, Dec. 21, 1968, *4*, 729–734. (From: The University of Melbourne, Department of Medicine and Cardiovascular Unit, St. Vincent's Hospital, Melbourne, Australia.)

Detailed clinical angiographic and hemodynamic findings are reported before, during, and after streptokinase therapy in 18 patients with major pulmonary embolism. In addition, detailed angiographic and hemodynamic changes after 24 hours of heparin administration are recorded in 3 patients.

The streptokinase was infused by catheter or given intravenously.

Fourteen patients showed clinical improvement, and 12 out of 16 patients angiographed showed definite angiographic improvement after 24 to 48 hours of treatment with streptokinase.

The angiographic improvement following streptokinase contrasted with the lack of this in 3 patients after 24 hours of heparin treatment. Resolution following streptokinase therapy was most noticeable in patients treated shortly after a single embolic episode and was least marked in those with recurrent embolism complicated with associated cardiac or pul-

monary disease. Of the 4 patients who failed to improve, 2 died and 2 had pulmonary embolectomy and survived.

The clinical findings, cardiac catheter data, pulmonary function tests, treatment, clinical, and angiographic results are presented on all patients in table form. Serial angiograms are presented in 5 cases.

The mean loading dose of streptokinase was 160,000 units, with the range of 30,000 to 250,000 units. The maintenance dose per hour ranged from 20,000 to 200,000 units with a mean of 90,000 units and the mean time of infusion was 36.5 hours at a range of $1\frac{1}{2}$ to 72 hours. Coagulation assays and plasma fibrinolytic activity were monitored. Complications including local bleeding from the site of brachial artery puncture occurring in 5 patients and more serious bleeding occurring in 3 patients are discussed.

The results suggest that streptokinase therapy is practicable, provided that adequate laboratory control is available, and that it hastens early resolution in acute major pulmonary embolism.—*William T. Mc Laughlin, M.D.*

Moraski, R. E., Sandler, I. A., O'Hern, J. A., and Bousvaros, G. Evaluation of right atriography for the detection of pericardial effusion. *Am. J. M. Sc.*, Dec., 1968, *256*, 360–367. (Address: Dr. George Bousvaros, Cardiology Department, Veterans Administration Hospital, Albany, N. Y. 12208.)

Twenty-three patients with roentgenologically large cardiac shadows were studied for the presence of pericardial effusion by taking serial anteroposterior roentgenograms in inspiration at 2 per second for 3 seconds in the right lateral decubitus position, beginning at the end of the intravenous injection of 40 cc. of 50 per cent hypaque. The injection was made by hand using a metal cased syringe. The focal film distance was 120 cm.

The distance between the outlined dependent part of the right atrial cavity and the lowermost part of the cardiac silhouette was found to be between 4 and 11 mm. in 12 patients who were considered not to have pericardial effusion. In 6 patients with effusion (proven by pericardiocentesis or biopsy in 4) the extra-atrial shadow ranged between 22 and 48 mm. Fibrinous or adhesive pericarditis was found in 3 cases with extraluminal bands between 12 and 16 mm. The results of the technique were unsatisfactory in 2 patients.

It is concluded that the method is technically simple and virtually diagnostic of significant pericardial effusion when the extra-atrial thickness is over 20 mm.—*William T. Mc Laughlin, M.D.*

Postlethwait, R. W., Kim, Seuk K., and Dillon, M. L. Esophageal complications of vagotomy. *Surg., Gynec. & Obst.*, Mar., 1969, *128*, 481–488. (From: The Departments of Surgery and Radiology, Veterans Administration Hospital and Duke Medical Center, Durham, N. C.)

The complications most likely to develop as a result of operative injury from vagotomy are perforation, devascularization, or periesophageal hemorrhage. Postoperative dysphagia may be due to neurogenic disorder, edema and hematoma formation, periesophageal fibrosis or esophagitis. Hiatal hernia is usually a late complication.

The incidence of perforation is very low, only 0.54 per cent. In this series of 24 perforations, 18 were recognized at surgery and closed. Only 3 deaths occurred in the unrecognized perforations. Extensive dissection can result in impaired blood supply and delayed perforation, especially if infection is present. Postoperative hemorrhage is rare. Dysphagia is also rare and transient, the incidence being only 3.6 per cent. Paraesophageal fibrosis can occur rapidly after surgery, but it is also very rare. The authors found the incidence of postoperative hiatus hernia to be 11 per cent. However, none of these were symptomatic.—*Arch H. Hall, M.D.*

RADIOISOTOPES

Poe, Norman D., Dore, Earl K., Swanson, Leonard A., and Taplin, George V. Fatal pulmonary embolism. *N. M. J. Nuclear Med.*, Jan., 1969, *10*, 28–33. (Address: Dr. Norman D. Poe, Laboratory of Nuclear Medicine, 900 Veteran Avenue, Los Angeles, Calif. 90024.)

The authors scanned over 700 patients suspected of having pulmonary embolism in the past 4 years. There were 7 deaths in this group in which the primary cause of death was massive pulmonary embolism. The 7 death cases are presented in detail.

A dose of 180 to 350 μc I^{131}-labeled macroaggregated human serum albumin was injected intravenously into an antecubital vein with the patient being upright. The posterior scanning was begun immediately, followed by anterior and/or lateral scannings, as needed. Critically ill patients were brought to the department in their hospital beds, and the I^{131} was given with the patient being recumbent or in a semi-recumbent position. Usually only an anterior scanning was done.

The scannings were performed using scanners with a 3×2 or 5×2 inch NaI (Tl) crystal at speeds of 60 to 200 cm. per minute.

Major or fatal pulmonary embolization was rarely found to be the first evidence of a thrombo-embolic process in over 300 cases of pulmonary embolism with positive lung-scan findings. Most patients had symptoms or signs for 5 to 7 days or more preceding the fatal attack.

Lung scanning is an effective and widely applicable test for identifying occlusion of lobar, segmental or subsegmental pulmonary arteries. Adequate anticoagulation is known to definitely reduce the incidence and mortality from recurrent emboli. Detection of the minor emboli by lung-perfusion scanning followed by intensive anticoagulation is a potentially effective means of preventing massive embolization.—*Charles W. Cooley, M.D.*

FLANC, C., KAKKAR, V. V., and CLARKE, M. B. The detection of venous thrombosis of the legs using ^{125}I-labelled fibrinogen. *Brit. J. Surg.*, Oct., 1968, *55*, 742–747. (From: The Department of Surgery, King's College Hospital Medical School, London, England.)

A study of 96 patients was made to establish the value of I^{125}-labelled fibrinogen as a diagnostic test for deep vein thrombosis.

Two groups of patients were studied: (1) Postoperative group (65 patients). In these the test was performed to detect venous thrombosis at its earliest stage. (2) Diagnostic group (35 patients). These presented with clinical signs of deep vein thrombosis and the radioactive fibrinogen test was used to confirm the diagnosis.

The thyroid gland was blocked by sodium iodide prior to the injection of I^{125}-fibrinogen (100 microcuries) into an arm vein. The radioactivity was measured over the legs 1 hour after the injection.

(1) In the postoperative group, counting was first performed on the day before operation; this provided a base-line for comparison with subsequent measurements of radioactivity. Counting was repeated when the patient returned from the operating theater and on the third and sixth days.

Four patterns of radioactivity occurred in the postoperative group: (a) normal; (b) early transient rise; (c) early sustained rise; and (d) late rise.

Phlebographies were performed in those patients showing increased radioactive counts or clinical signs of thrombosis. The phlebograms were normal in each of 7 showing early transient rises. Thrombi were seen in 7 of the 8 limbs with early sustained rises and in each of the 10 limbs showing the late rise.

(2) In the diagnostic group a positive diagnosis of deep vein thrombosis was made if the radioactive counts became raised over the limb.

In this study increased radioactive counts in a leg developed in half of the patients after operation. The true incidence of deep venous thrombosis confirmed by phlebography was 35 per cent. In half of these patients increased radioactivity was detected on their return from the operating theater, suggesting that thrombi first developed during the operation. Of the postoperative patients with confirmed deep vein thrombosis, only 50 per cent had clinical signs; in the remaining 50 per cent there were no symptoms or signs of deep vein thrombosis.

The results of this study show that the radioactive fibrinogen technique, when used routinely after operation, is the most sensitive method for the earliest diagnosis of venous thrombosis.—*A. Franklin Turner, M.D.*

O'MARA, R. E., MCAFEE, J. G., and SUBRAMANIAN, G. Rare earth nuclides as potential agents for skeletal imaging. *N. M. J. Nuclear Med.*, Jan., 1969, *10*, 49–51. (From: Upstate Medical Center, State University of New York, Syracuse, N. Y.)

The nuclides used presently for skeletal imaging are Sr^{85}, F^{18} and Sr^{87m}. They are high energy gamma emitters and are not well suited for the Anger camera. The detection efficiency of the rectilinear scanner is lower with high energy gamma emitters than with weaker gamma emitters. The physical half lives of the above nuclides are at the extremes with Sr^{85} being long and F^{18} and Sr^{87m} being very short.

Citrate complexes of the heavier lanathons concentrate primarily in bone, whereas the lighter lanathons (Ce to Gd) localize primarily in the liver.

The biologic localization of rare earths is altered by chelation. HEDTA (hydroxyethylenediamene tetracetic acid) forms chelates of intermediate stability and about 50 per cent of the administered dose localizes in the skeleton.

Four possible bone imaging agents from the heavier lanathon group as HEDTA chelates (lutetium [Lu^{176m} and Lu^{177}], samarium [Sm^{153}] and erbium [Er^{171}]) were evaluated. Sm^{153} and Er^{171} were found to be best suited for skeletal imaging. Sm^{153} has the advantage of a greater convenience because of a half life of 47 hours and a higher efficiency with the Anger camera. Er^{171} has the advantage of a lower radiation dose and a higher ratio of external photons per disintegration.

The above nuclides are readily and cheaply produced in a nuclear reactor without significant radioactive impurities.—*Charles W. Cooley, M.D.*

CAMPIONE, KENNETH M., and STEINER, SHELDON H. Analysis of precordial isotope dilution curves obtained after antecubital and intracardiac injection. *N. M. J. Nuclear Med.*, Dec., 1968, *9*, 630–633. (From: Northwest University Medical Center, Chicago Wesley Memorial Hospital and Passavant Memorial Hospital, Chicago, Ill.)

Cardiac output can be estimated by analyzing the primary passage curve obtained from external precordial isotope counting of I^{131}-labeled human serum albumin injected into an antecubital vein and by using the blood volume calculated by isotope dilution.

Cardiac outputs obtained by the above method were compared with simultaneous direct Fick out-

puts. The curve of the primary passage after antecubital injection was analyzed to determine the transit time from the right heart peak to the left heart peak. This time was compared with the pulmonary artery pressure. Circulation times measured from the time the isotope appeared in the heart to the time it appeared in the head after antecubital and left ventricular injections were analyzed. The difference between the two circulation times is an estimate of the transit time from the right heart to the left heart. A comparison was then made with the main pulmonary artery pressure.

The authors used 15 to 20 μc of I^{131}-labeled human serum albumin for the antecubital vein injection, and 10 to 15 μc of I^{131}-labeled hippuran for the catheter injection.

The external precordial isotope dilution method with antecubital injection of I^{131}-labeled human serum albumin for calculating cardiac index compared favorably with the results of the Fick method. The method did not correlate well with the cardiac output obtained by the Fick method when the injections were made into the cardiac chambers, and one or more of the cardiac chambers or the pulmonary circulation was bypassed.

The right and left heart transit time (the time from the peak count of the radioisotope into the right heart to the time of the peak count into the left heart obtained by precordial detection after antecubital injection) did not correlate well with the mean pulmonary artery pressure. The difference between the heart to head circulation time after antecubital and left ventricular injection (which is a measure of the right heart to left ventricular transit time) correlated well with the mean pulmonary artery pressure.—*Charles W. Cooley, M.D.*

Hisada, Kin-Ichi, Mishima, Tsutomu, Hiraki, Tatsunosuke, Tonami, Norihisa, Matsudaira, Masamichi, and Kuranishi, Makoto. Intravenous radioisotope angiography using ^{113m}InFe DTPA-ascorbic acid. *Radiology*, Dec., 1968, *91*, 1204–1207. (From: Department of Radiology, School of Medicine, Kanazawa University, Takara-machi 13-1, Kanazawa, Japan.)

The authors describe a method of providing morphologic information similar to roentgen-ray angiography by means of the gamma ray scintillation camera and a single intravenous injection of a large dose of a short lived nuclide.

A prepared dose of 6 to 12 mc of In^{113m}FeDTPA-ascorbic acid is injected into the antecubital vein or a superficial dorsal vein in the hand. Immediately afterwards serial scintiphotographs of 2 to 8 second duration are made of the kidneys and heart. The first scintiphotograph shows the vascular phases corresponding to the arterial, the nephrographic, and venous blood phases demonstrated in renal angiograms. These 3 phases cannot be distinguished by the present technique. In the later functional phase, the In^{113m} activity has disappeared from the abdominal aorta, and the kidney is visualized by the transient accumulation of In^{113m}FeDTPA-ascorbic acid. Renal contours are best delineated 4 minutes after injection. The vascular phase demonstrates an area involved by such a vascular tumor as a hypernephroma, and the functional phase shows filling defects in the lesion. Avascular lesions such as renal cysts give a constant filling defect in both phases.

The technique is simple, atraumatic, and without the undesirable pharmacologic effects sometimes seen in cases of contrast medium (iodine) idiosyncrasy.—*L. H. Deiterman, Ph.D.*

MISCELLANEOUS

Presberg, Harry J., and Singleton, Edward B. Combined immune deficiency disease: its radiographic expression. *Radiology*, Nov., 1968, *91*, 959–964. (From: Texas Children's Hospital, 6621 Fannin Street, Houston, Texas 77025.)

The authors deal with the roentgenographic manifestations of deficiency in the immune mechanism. These roentgenographic findings are related to atrophic lymphoid tissue and abnormal response to infections and are indicative of basic stem cell defects. Findings are present in the nasopharynx, mediastinum, lungs, and gastrointestinal tract.

Nasopharynx. No lymphoid tissue is seen in the nasopharynx. A lateral roentgenogram of the neck should be part of any workup. Good standards of normality have not been set for any age and evaluation prior to 1 year is difficult.

Thymus. The thymus somehow mediates cellular immune functions. Abnormalities in the immune mechanism will be reflected in variation in size of the gland. A small thymus gives an "empty" anterior mediastinum on a lateral chest roentgenogram. However, involution from other causes cannot be distinguished from dysgenesis.

Lungs. Pulmonary infection is usually the terminal event and a common agent is *Pneumocystis carinii.*

Gastrointestinal tract. Clinically, vomiting and diarrhea are often present. There is no specific gas or mucosal pattern, with some nonspecific dilatation of bowel loops being present. There is no nodular hyperplasia which may be seen in dysgammaglobulinemia. Monilial esophagitis, if it is present, is a good indication of immune abnormality.—*J. P. Eberts, M.D.*

Anghileri, Leopoldo J., and Dogan, Erdal B. Prevention of abdominal metastases after intraperitoneal injection of Yoshida ascites cells: use of a new colloidal ^{32}P-chromic phosphate. *N. M. J. Nuclear Med.*, Nov., 1968, *9*, 562–566. (From: Deutsches Krebs-

forschungszentrum, Institut für Nuklearmedizin, Heidelberg, Germany.)

Numerous investigators have described the utilization of various chemotherapeutic agents at the time of and after surgery to decrease the incidence of postoperative liver metastases. Because of the high toxicity of these compounds, their use requires extreme caution. P^{32}-chromic phosphate has the advantages of the lack of bone marrow depression in the proposed use as a radiation prophylaxis following surgical tumor removal. The authors have studied the ability of this compound to prevent metastases in the abdominal cavity in rats following intraperitoneal injection of Yoshida ascites tumor cells.

A single injection of 50–75 μc of the P^{32}-chromic phosphate considerably reduces the metastases after a 7 day incubation period (control group: 90–100 per cent "take;" treated group 20–30 per cent). After 15 days the animals showed an increase in metastases but this increase was considerably less than in the survivals of the control group.

According to the experimental results, a considerable decrease in the metastatic incidence is obtained with a relatively low therapeutic dose (50–75 μc). A three-dose treatment schedule (after 20 minutes, 3 days and 6 days) resulted in significantly prolonged survival as well as fewer metastases.

From these results it can be stated that the colloidal form of P^{32}-chromic phosphate prepared by the authors' technique has distinct advantages over the classical particulate form.—*Luther W. Brady, M.D.*

Gunz, F. W., and Spears, G. F. S. Distribution of acute leukaemia in time and space: studies in New Zealand. *Brit. M. J.*, Dec. 7, 1968, *4*, 604–608. (From: The Pathology Department, Christchurch Hospital, Christchurch, and the Department of Preventive and Social Medicine, University of Otago, Dunedin, New Zealand.)

The distribution of leukemia in time and space was examined by tracing the date of onset and the place of residence in all cases of childhood leukemia and of acute leukemia in adults, totaling 1,003 cases, which occurred in New Zealand during the 12 years from 1953 to 1964.

Significant seasonal variations in the onset were found in adults but not in children. Time-space clustering did not occur in adults, but a significant tendency towards it was found in children less than 6 years of age. Since a similar tendency has previously been found by two other groups of investigators, it is suggested that leukemia in young children may have a different etiology from that occurring at other ages.

It is suggested that future surveys of leukemia clusters might, with advantage, be confined to the group most likely to show the effect—children under the age of 6 years.—*A. Franklin Turner, M.D.*

Paul, Freda M. Childhood leukaemia in Singapore children. *Singapore M. J.*, Sept., 1968, *9*, 139–150. (From: Department of Paediatrics, University of Singapore, Singapore.)

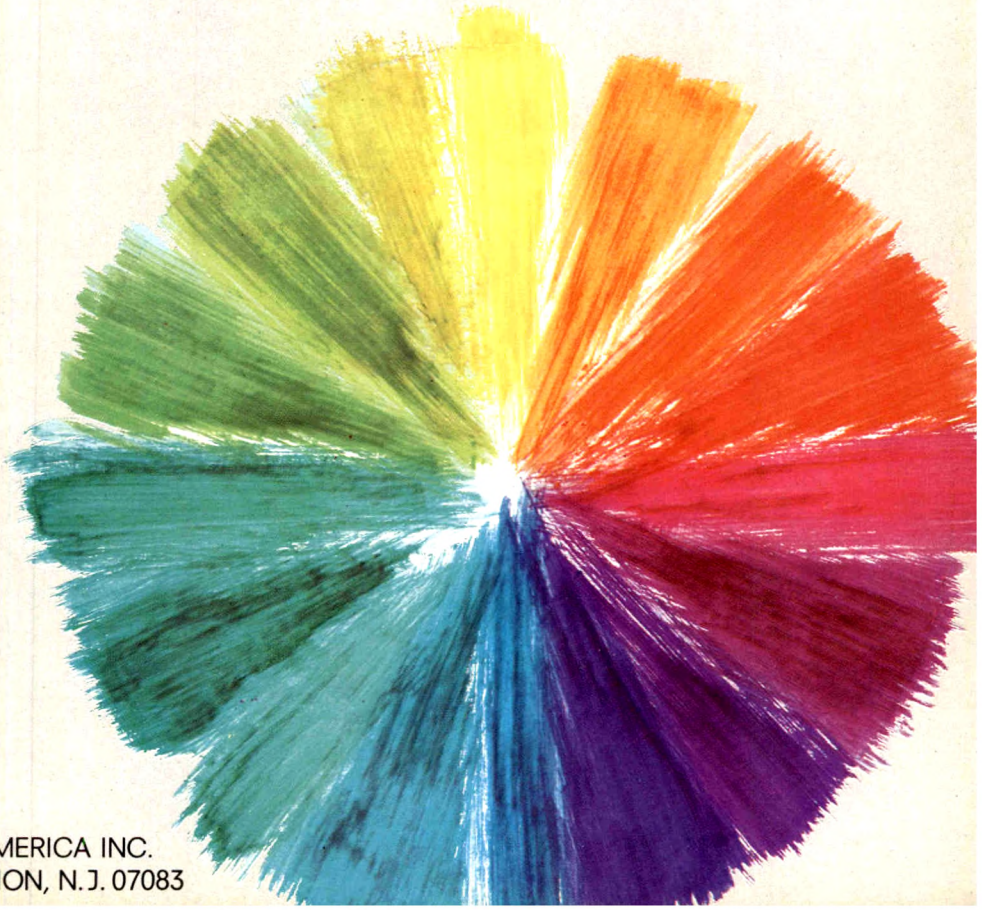
The author presents a review of childhood leukemia. She briefly discusses the incidence, mortality, distribution, etiology, roentgenologic changes and treatment.

The roentgenologic changes are metaphyseal translucent zones, focal bone erosions, diffuse bone infiltration, subperiosteal ossification and osteosclerosis.—*Richard P. Taylor, M.D.*

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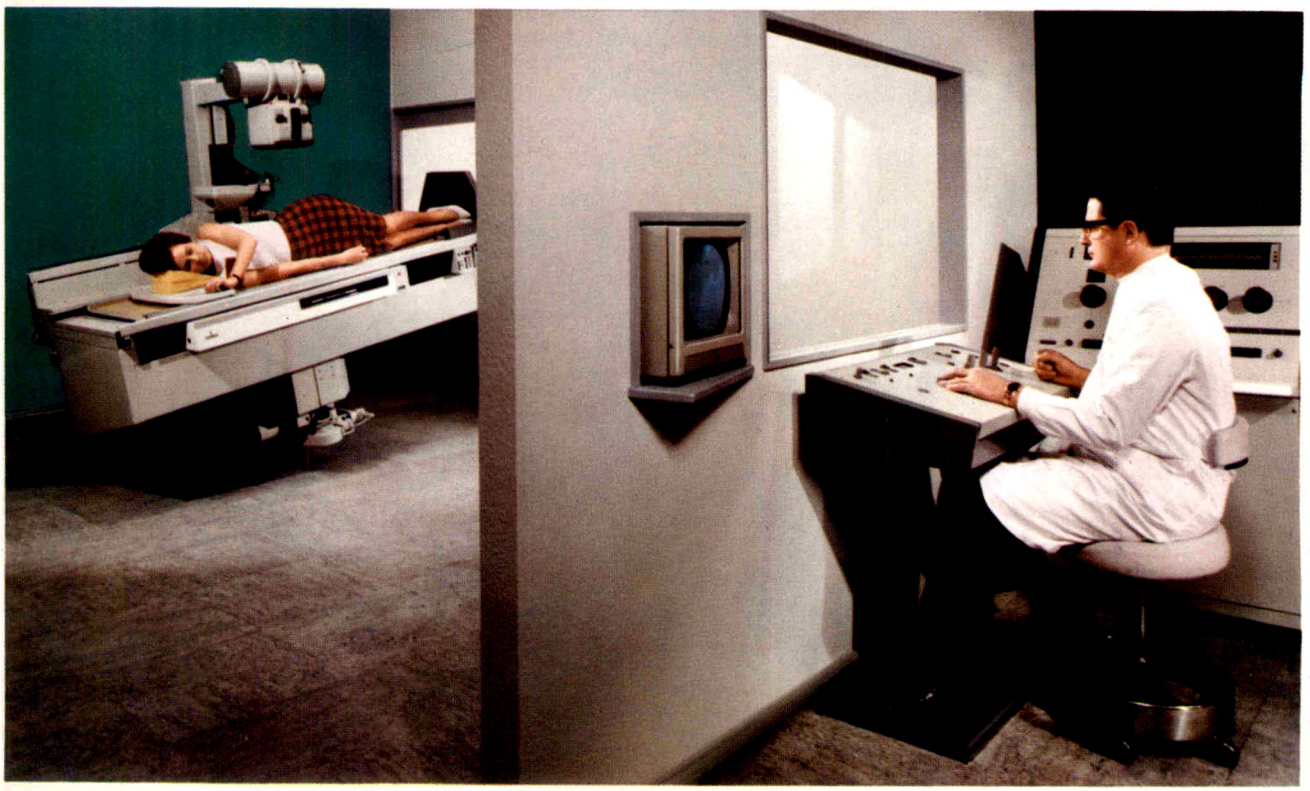
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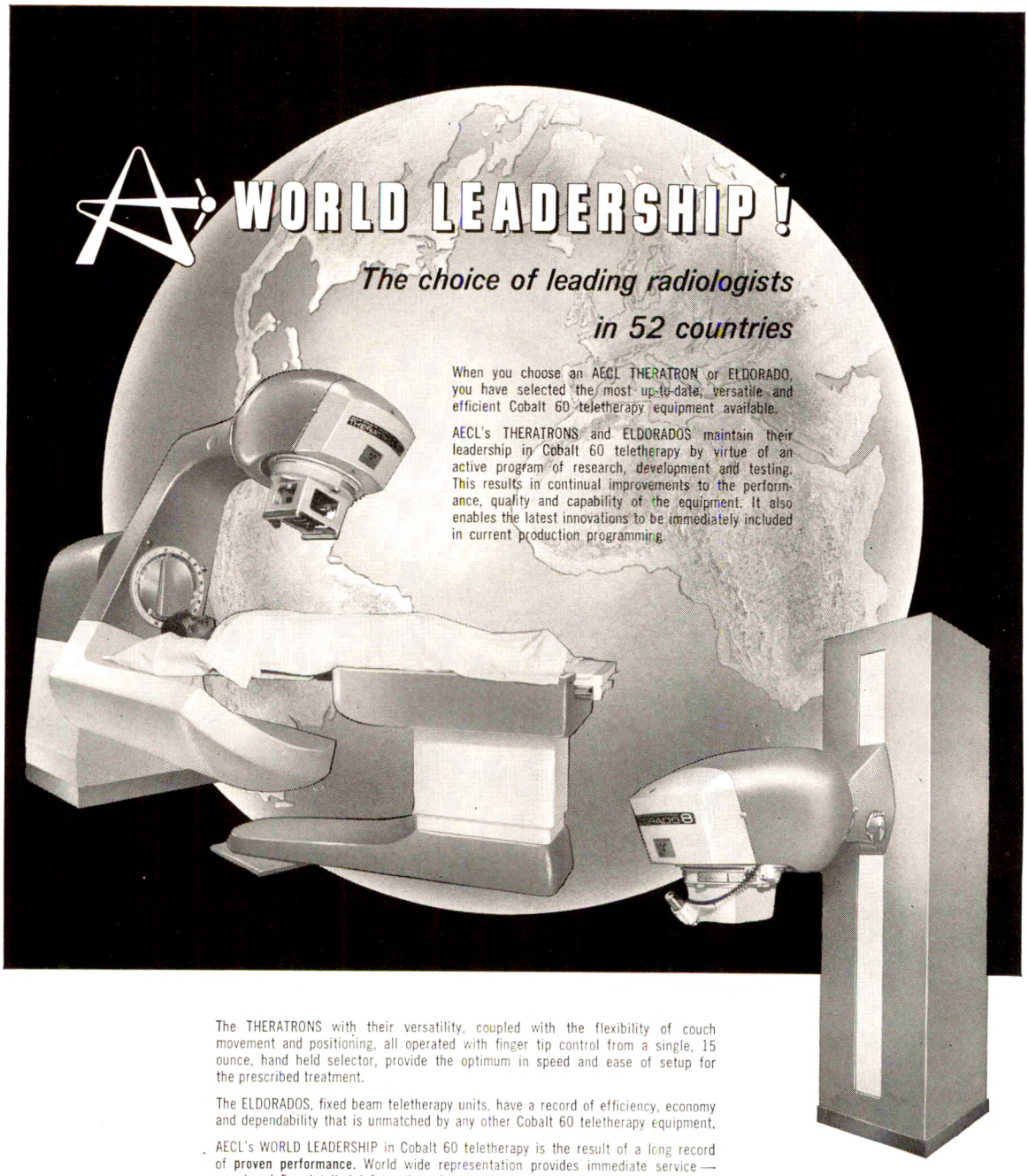
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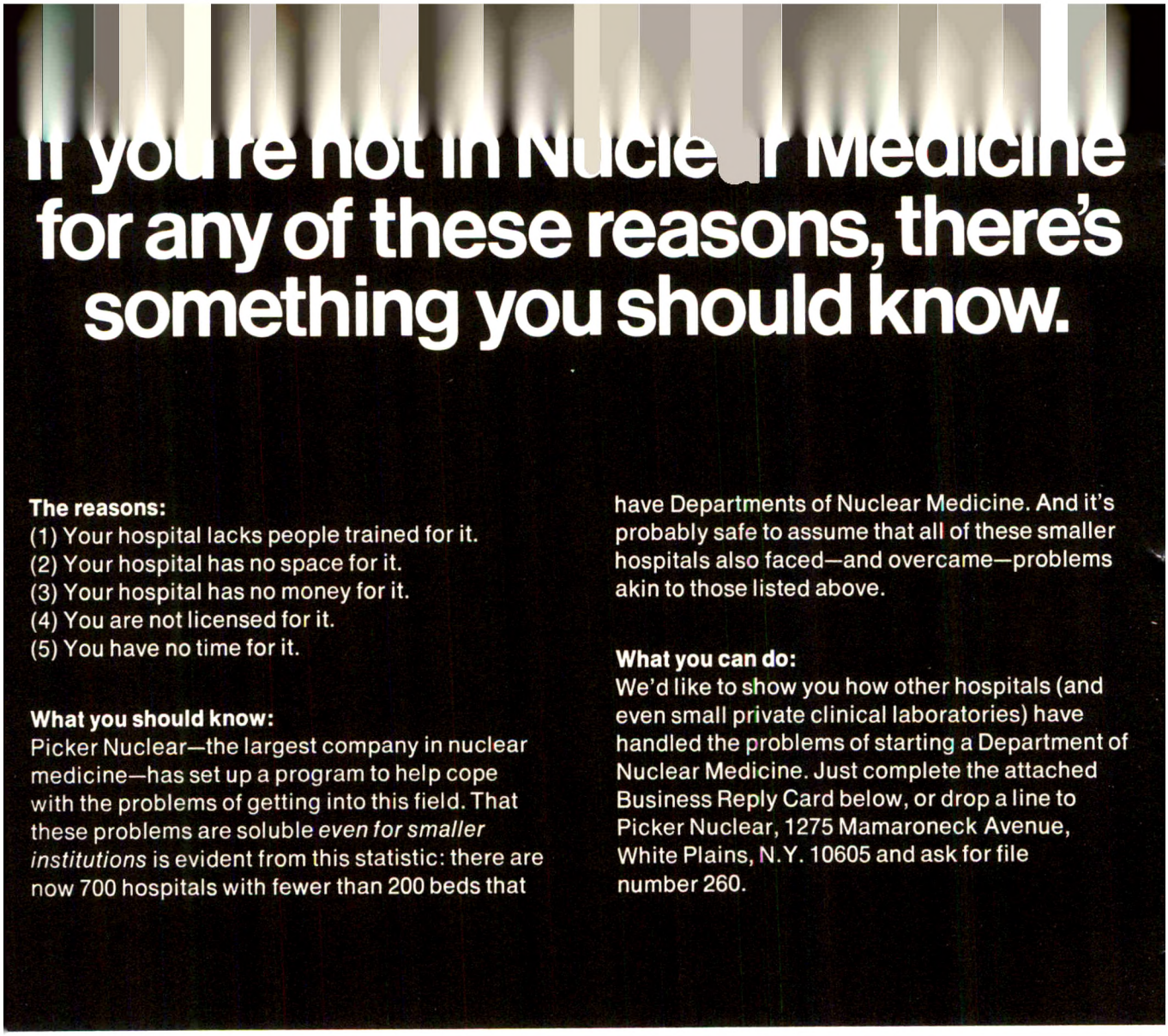
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SQUIBB

a research concept in contrast visualization

for better definition of disease: documenting differences between contrast agents

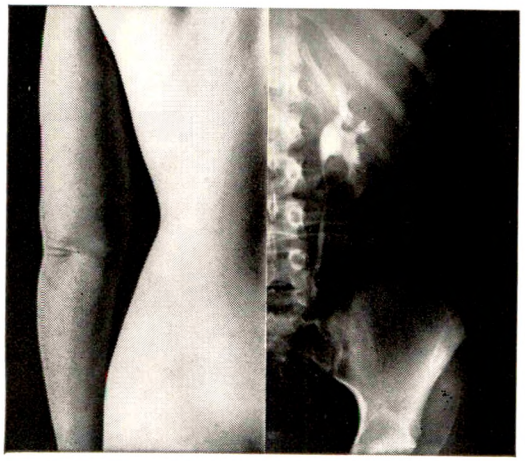
No. 1 in a series:

Renografin-60 (meglumine diatrizoate injection) preferred in a study of pyelographies of 2,234 patients.

In a new large scale study,[1] "...to determine which medium would produce adequate visualization of the urinary tract with the fewest toxic effects on the patient," Macht *et al.* have compared Renografin-60 with 2 other contrast agents.

Data were analyzed in 2,234 unselected (consecutive) patients, according to age, sex, and general disease group for the study population as a whole. The first 683 patients received 50% diatrizoate sodium solution, the next 921 patients received Renografin-60, and the final 630 patients received 66.8% sodium iothalamate solution.[1]

criteria for quality and comparative safety The contrast agents were evaluated for quality of diagnostic films as follows: films showing a dense concentration of contrast medium with filling and visualization of all major and minor calyces, infundibula, pelves and almost all of each ureter were listed as "good"; films showing less concentration with incomplete visualization of all portions of urinary tract but sufficient to produce diagnostically adequate films were listed as "fair"; films showing unsatisfactory visualization of urinary tract, or films which could not be interpreted, as "poor." The media were also evaluated as to incidence of the following side effects: nausea, vomiting, fainting, shock or severe reaction, hiccups, hives, pain in arm, sneezing, hot flushes, stuffiness of nose or ears.[1]



The following chart* shows comparative results of the 3 media according to age category:

quality of pyelograms and side effects expected in standard population of 1,000 patients by age, according to type of medium used

medium used and type of patient	standard population	quality of pyelograms good	fair	poor	with side effects
meglumine diatrizoate					
all ages,	1,000	827	123	50	41
0-19†	126	122	3	1	3
20-49	415	374	35	6	27
50-69	315	240	51	24	9
70 or older	144	91	34	19	2
diatrizoate sodium					
all ages,	1,000	782	134	84	72
0-19	126	115	6	5	7
20-49	415	378	26	11	40
50-69	315	227	64	24	19
70 or older	144	62	38	44	6
sodium iothalamate					
all ages,	1,000	883	81	36	54
0-19	126	122	4	0	7
20-49	415	393	20	2	29
50-69	315	269	32	14	13
70 or older	144	99	25	20	5

*Adapted from Macht[1] †In some patients in this age group, higher than recommended doses were used.

In theory: "The choice of contrast agent should ideally be individualized according to the age, sex, and disease group of the patient in order to obtain a high probability of complete visualization of the urinary tract with low probability of adverse side effects."[1]

In practice: "The choice is to be made...on the basis of the agent which gives the best concentration and the fewest side effects in the greatest number of patients regardless of age, sex, or disease category."[1]

In order of preference: Although Renografin-60 was not rated highest in all categories, the authors feel that their preference of the contrast media for intravenous pyelography would be: first, Renografin-60; second, sodium iothalamate; third, diatrizoate sodium.[1]

For brief summary of prescribing information, please refer to the end of this advertisement.

definition of safety...

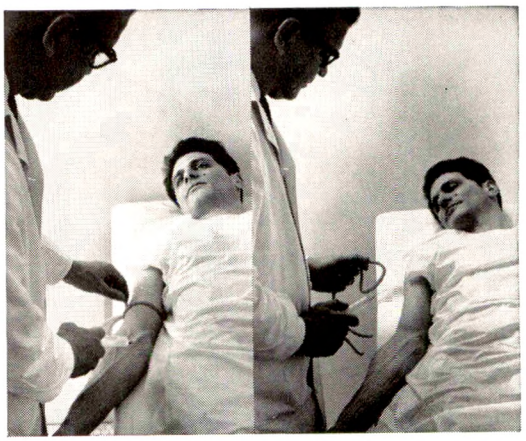
demonstrated in animals... Since meglumine diatrizoate is also used for cerebral angiography, toxicity studies of administration via the carotid artery are therefore of interest. Fischer and Eckstein[2] designed angiographic studies in animals in which procedures were very similar to clinical angiography, and which yielded data that was quantitative, graphic and nonsubjective.[2] According to the authors: "We selected the alterations in arterial blood pressure, venous pressure, heart rate and rhythm, the electrocardiogram and end-expiratory CO_2 concentration resulting from experimental cerebral angiography as refined, sensitive indications of the toxicity of a particular contrast material."[2] Their results of measured cardiovascular functions in dogs indicated that meglumine diatrizoate was far less toxic than four other contrast media.[2] As Fischer and Cornell reported in a later study: "Despite the testing of more highly concentrated solutions and larger doses, the cardiovascular responses [in dogs] from methylglucamine [meglumine] salts were much less than from sodium salts, an observation consistent with previous experiments."[3]

Other investigators have documented the comparative safety of meglumine salts in experimental studies. In order to determine reaction and tolerance of the intestines, Cooley[4] injected meglumine diatrizoate into mesenteric arteries of dogs and found no damage. Gensini *et al.*[5] reported that cardiovascular responses with it were almost identical to blood transfusions.

theory of lower toxicity with meglumine... Gensini and DiGiorgi have offered a hypothesis to explain their findings of lesser toxicity with experimental intravascular injections of methylglucamine (meglumine) salts. "When a relatively undiluted amount of sodium salts of a contrast agent is injected in an artery and carried by the blood stream toward the capillary bed, its molecules rapidly dissociate and readily diffuse through the capillary membrane and into the tissue. There, both the toxic effect of the iodine-containing organic radical and the increased concentration of sodium will readily manifest themselves. At equal concentrations of sodium, the end results will closely reflect the intrinsic toxicity of the iodine-containing organic radical on the tissues...."[5]

"In the case of the methylglucamine compounds, the same dissociation takes place. However the larger methylglucamine molecule, rich in hydrogen bonds, apparently either limits the migration of the organic radicals outside the vessel or at least minimizes their effects on the cellular metabolism."[5]

proved in practice... Paralleling similar findings in animals, clinicians have reported a generally lower



incidence of untoward reactions with Renografin-60 in urologic and cerebrovascular use. However, as with all intravascularly injected contrast agents, the possibility of severe reactions should be kept in mind (see Contraindications, Precautions and Side Effects below). In one study of over 600 urologic patients, the investigators reported that Renografin-60 produced urograms of diagnostic quality with a 6% incidence of side effects. The authors concluded: "It is hard to believe that any drug introduced intravenously could be so well borne by so many patients...."[6]

In a 74-patient study,[7] comparing Renografin-60 with diatrizoate sodium in carotid arteriography, Shealy commented: "With confused patients who are to have arteriography under local anesthesia, it is particularly desirable to have an agent that causes little pain." In this study, since "...60 per cent Renografin has resulted in considerably less pain than 50 per cent or 45 per cent [diatrizoate sodium]...we have converted to the routine use of 60 per cent Renografin for carotid arteriography; an additional 1,500 arteriograms done with 60 per cent Renografin have been quite satisfactory."[7]

better tolerated even in pediatrics... Citing some difficulties in administering contrast agents intravenously to children, Strasser *et al.*[8] selected Renografin-60 for intramuscular use in excretion urography in 16 pediatric patients because of the mild and relatively few reactions consistently associated with its use. The authors concluded: "The almost complete absence of any kind of local effect from its injection into the gluteal muscle and the absence of any serious reactions, local or systemic, indicate the safety of the medium."[8]

For brief summary of prescribing information please refer to the end of this advertisement.

definition of efficacy...

a thoroughly investigated meglumine salt Extensively evaluated for over a decade, Renografin has been consistently shown to yield a high percentage of diagnostic quality films in many phases of contrast visualization.

Upon intravenous injection, Renografin is rapidly carried to the kidneys and is so well concentrated that renal passages—including renal pelvis, ureters and bladder—may be clearly visualized. This medium also provides high contrast vasography in visualization of the cerebral vessels and the peripheral arteries and veins.

proved diagnostic excellence... In a comparative study[9] of 3 contrast agents used in cerebral angiography by Doehner (comprising a cross section of an average neurosurgical practice), Renografin-60 was equal in the arterial phase and slightly superior in the venous phase of the examination.

Findings of a previously cited study by Orr *et al.*,[6] in intravenous pyelography, also attest to the diagnostic excellence of Renografin-60. "Satisfactory roentgenograms of the kidneys were obtained in 636 (97%) of the cases, demonstrating the great diagnostic value of this procedure." And, as noted previously, Shealy found the contrast agent to be "quite satisfactory" in 1,500 carotid arteriograms.[7]

References: 1. Macht, S. H.; Williams, R. H., and Lawrence, P. S.: Amer. J. Roentgen. *98*:79 (Sept.) 1966. **2.** Fischer, H. W., and Eckstein, J. W.: Amer. J. Roentgen. *86*:166 (July) 1961. **3.** Fischer, H. W., and Cornell, S. H.: Radiology *85*:1013 (Dec.) 1965. **4.** Cooley, R. N., *et al.*: Angiology *15*:107 (Mar.) 1964. **5.** Gensini, G. G., and DiGiorgi, S.: Radiology *82*:24 (Jan.) 1964. **6.** Orr, L. M.; Campbell, J. L., and Thomley, M. W.: J.A.M.A. *169*:1156 (Mar.) 1959. **7.** Shealy, C. N.: J. Neurosurg. *20*:137 (Feb.) 1963. **8.** Strasser, N. F., *et al.*: Radiology *79*:408 (Sept.) 1962. **9.** Doehner, G. A., and Brugger, G. E.: New York J. Med. *60*:4022 (Dec.) 1960.

Contraindication

A history of sensitivity to iodine per se or to other contrast media is not an absolute contraindication to the use of meglumine diatrizoate.

Precautions and Side Effects

Severe, life-threatening reactions are rare; when they occur they suggest hypersensitivity. A personal or family history of asthma or allergy warrants special attention and may predict, more accurately than pretesting, the likelihood of a reaction, although not the type nor severity of the reaction in the individual.

The value of any pretest is questionable. The pretest most performed is the slow injection of 0.5-1.0 cc. of the preparation into a peripheral vein. An impending reaction is often indicated by transient burning and flushing, pain, "jump-like" reactions, respiratory difficulty, faintness, sneezing, itching, nausea, vomiting or urticaria. Should the test dose produce an untoward response, the necessity for continuing the examination should be re-evaluated. Antiallergic drugs may be used to advantage. In a few cases, the reactions to the test dose have been extremely severe.

The more serious anaphylactoid reaction requires immediate treatment and may occur despite a negative sensitivity test. An emergency tray consisting of vasopressor drugs, epinephrine hydrochloride 1:1000, methoxamine (Vasoxyl) or metaraminol bitartrate (Aramine), and glucose and saline is recommended. Oxygen and instruments to guarantee a clear airway must be readily available.

Caution must be exercised, especially in cerebral angiography in extreme age, in severely debilitated patients and in those with marked or severe hypertension, advanced arteriosclerosis, cardiac decompensation, recent cerebral embolism, or thrombosis, chronic pulmonary emphysema and in cyanotic infants.

For full details the Package Insert should be read.

Supply: Renografin-60 is supplied in vials and ampuls as a sterile aqueous solution providing 60% meglumine diatrizoate containing approximately 29% firmly bound iodine.

Available in 30 cc. vials or 25 cc. ampuls.

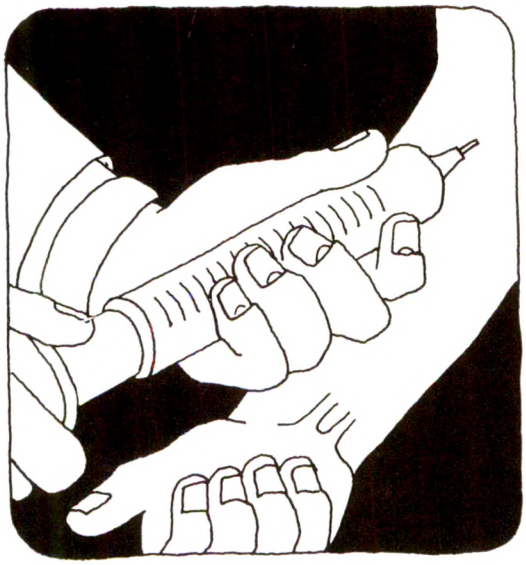
in excretion urography
cerebral angiography
peripheral arteriography
and venography

Renografin®-60

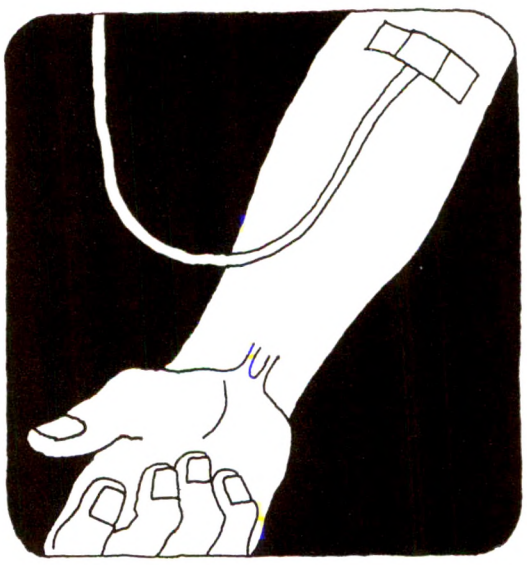
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*By diluting the 50% solution with an equal amount of sterile water for injection, USP, sodium chloride injection, USP, or dextrose injection, 5%, USP.

(Please see summary on following pages)

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sodium
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Excretory Urography and Drip Infusion Pyelography

Description: Hypaque sodium is a sterile aqueous solution of sodium 3,5-diacetamido-2,4,6-triiodobenzoate, a radiopaque medium used to delineate internal structures.

Warning: Do not use Hypaque sodium for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

General and Specific Precautions: Caution is advised in patients with a history of bronchial asthma, other allergic manifestations, or of sensitivity to iodine; these conditions represent a special risk, though not an absolute contraindication. To avoid or minimize possible allergic reactions, premedication with antihistamines may be considered. Benadryl (diphenhydramine hydrochloride) in the same syringe with Hypaque may result in precipitation. A test dose of contrast medium is not entirely reliable. Severe reactions, including fatalities, have occurred with a test dose as well as with the full diagnostic dose.

Caution is advised in patients with severe cardiovascular disease. In patients with impaired renal function and cardiovascular disease, drip infusion pyelography imposes a sudden osmotic and sodium load which can precipitate congestive heart failure. Contrast media injected into arteries or veins can promote sickling of red cells in susceptible individuals. In patients with reduced renal function, repeat of excretory or retrograde pyelography should be delayed at least 48 hours to avoid temporary suppression of urine. In preparation for excretory urography of patients with multiple myeloma, partial dehydration is not recommended, since this may predispose to the precipitation of myeloma protein in the kidney tubules. When thyroid function studies (PBI and 24-hour radioiodine uptake levels) are indicated, they should be performed *prior* to radiographic studies or several days afterwards, to avoid inaccurate results.

Hypaque sodium 50% should always be injected at body temperature.

General and Specific Adverse Reactions: Adverse reactions, usually of a minor nature, have occurred in 10-14 per cent of patients who have received Hypaque intravenously. Reactions due to *faulty technique* include hematomas and ecchymoses, following extravasation from the vein, and pyrogenic reactions. *Hemodynamic reactions* include vasodilatation with flushing, hypotension and, rarely, vein cramp or thrombophlebitis. Serious *cardiovascular reactions* include rare cases of cardiac arrhythmias (e.g., ventricular fibrillation), shock, and cardiac arrest. Transient proteinuria may occur occasionally following the injection of radiopaques and, rarely, oliguria and anuria have been reported secondary to a hypotensive reaction. *Allergic reactions* include asthmatic attacks, nasal and conjunctival symptoms, cutaneous reactions such as urticaria and, rarely, anaphylactic shock, sometimes with fatal outcome. Severe reactions may also be manifested by signs and symptoms relating to the *respiratory system* (dyspnea, cyanosis, pulmonary or laryngeal edema), or to the *nervous system* (restlessness, confusion, or convulsions). *Other reactions* include nausea, vomiting, excessive salivation, anxiety, headache, and dizziness. Infrequently, "iodism" (salivary gland swelling) from organic compounds appears two days after exposure and subsides by the sixth day. Reactions to drip infusion pyelography may not appear until some hours after the examination.

Angiography (Peripheral Arteriography and Venography)

Precautions *(See also General Precautions):* Extreme caution is advised in considering peripheral arteriography in patients suspected of having thromboangiitis obliterans (Buerger's disease). Any procedure (even needling or insertion of a catheter) may induce a severe arterial and/or venous spasm. Caution is also advisable in patients with severe ischemia associated with ascending infection.

Adverse Reactions *(See also General Adverse Reactions):* In addition to those listed under General Adverse Reactions, are those due to arterial trauma during the procedure (i.e., needling, insertion of catheter, subintimal injection, perforation, etc.) as well as to the hypertonicity or effect of the medium; also reported are transient arterial spasm, extravasation, hemorrhage, hematoma with tamponade, injury to nerves proximal to artery, thrombosis (rare in venography; if vein is irrigated following injection), dissecting aneurysm, arteriovenous fistula, (e.g., with accidental perforation of femoral artery and vein during needling) transient leg pain from contraction of calf muscles in femoral arteriography; transient hypotension after intraarterial (brachial) injection, and brachial plexus injury with axillary artery injections.

Cerebral Angiography: Because of the special techniques required, it is recommended that Hypaque sodium be used for this purpose only by persons skilled and experienced in carrying out this procedure.

Contraindication: Carotid angiography should be avoided during the progressive period of a stroke, since this increases the risk of cerebral complications.

Precautions *(See also General Precautions):* Select patients for this procedure with care. Use the 50 per cent solution with caution in extreme senility (but not old age, *per se*); advanced arteriosclerosis; severe hypertension; and cardiac decompensation.

The diagnostic value of the procedure, according to many authorities, when employed early enough in locating lesions amenable to surgery, may outweigh the added risk to patients who have recently experienced cerebral embolism or thrombosis (stroke syndrome). A small number of postangiographic fatalities, including progressive thrombosis, have occurred in which the procedure did not appear to play a role. Patients with severe cerebrovascular disease may be examined primarily by indirect methods of angiography.

Care should be exercised to avoid contaminating catheters, syringes, needles, and contrast media with glove powder or cotton fibers.

Angiography is hazardous in subarachnoid hemorrhage. In migraine, the procedure can be hazardous because of ischemic complications, particularly if performed during or soon after an attack.

Adverse Reactions *(See also General Adverse Reactions):* The major sources of complications are faulty technique, occlusive atherosclerotic vascular disease, repeated injections of the contrast media, and higher doses than those recommended.

Untoward reactions are mostly mild and transient, although permanent visual field defects and deaths have been reported.

(continued on next page)

(continued from preceding page)

Hypaque® 50%
sodium
brand of **sodium diatrizoate**

Vascular reactions: flushing, vessel spasm, thrombophlebitis, and cutaneous petechiae.

Neurologic complications: transient cerebral blindness, neuromuscular disorders, convulsions, coma, hemiparesis, unilateral dysesthesias, visual field defects, aphasia, and respiratory difficulties.

Aortography

Precautions *(See also General Precautions):* Special caution is advised to avoid inadvertent intrathecal injection when using the translumbar technique. The incidence and severity of reactions or complications that may occur are influenced by: the care and experience with which the procedure is performed; the amount and type of medium used; the age and condition of the patient; and the premedication and anesthesia used. Since aortography is not without some danger, it should be performed only by those experienced in the technique. Wherever possible, repeated injections of the solution during a single study should be avoided.

Adverse Reactions *(See also General Adverse Reactions):* Renal damage and shutdown; neurologic complications such as transverse myelitis or paraplegia; cardiovascular complications such as shock, cardiac arrest or failure, coronary occlusion, arterial thrombosis, embolism, and perforation of vessels; extravasation or hemorrhage from the puncture site or retroperitoneal catheter perforation; necrosis of the intestinal wall; acute pancreatitis; deaths; diffuse cutaneous petechiae; subintimal injection and aortic dissection.

Intraosseous Venography

See General Precautions and Adverse Reactions. A general anesthetic is sometimes necessary since the method is painful. Occasionally, extravasation of the contrast medium from the needle into the soft tissue may occur.

Direct Cholangiography

Precaution *(See also General Precautions):* This procedure should be used with caution in the presence of acute pancreatitis, injecting no more than 5 to 10 ml. without undue pressure.

Adverse Reactions *(See also General Adverse Reactions):* These may be attributed to injection pressure or excessive volume of the medium, resulting in overdistention. Such pressure may produce a sensation of epigastric fullness, followed by moderate pain in the back or right upper abdominal quadrant, which will subside when injection is stopped.

Some of the medium may enter the pancreatic duct and cause a transient serum amylase elevation 6 to 18 hours later, without apparent ill effects. Pancholangitis resulting in liver abscess has been reported. Occasionally, nausea, vomiting, fever, and tachycardia have been observed.

Hysterosalpingography

Contraindications: Menstruation, active or imminent; infection in any part of the genital tract, including the external genitalia; pregnancy, known or suspected. Use not advised for six months after end of pregnancy, or 30 days after conization or curettement.

Precaution *(See also General Precautions):* Caution should be exercised in patients with known or suspected carcinoma to avoid possible spread of the lesion by the procedure.

Splenoportography

Precautions *(See also General Precautions):* Procedure should be performed with caution on patients with blood dyscrasias, a tendency to severe bleeding, or a spleen recently become tender and palpable.

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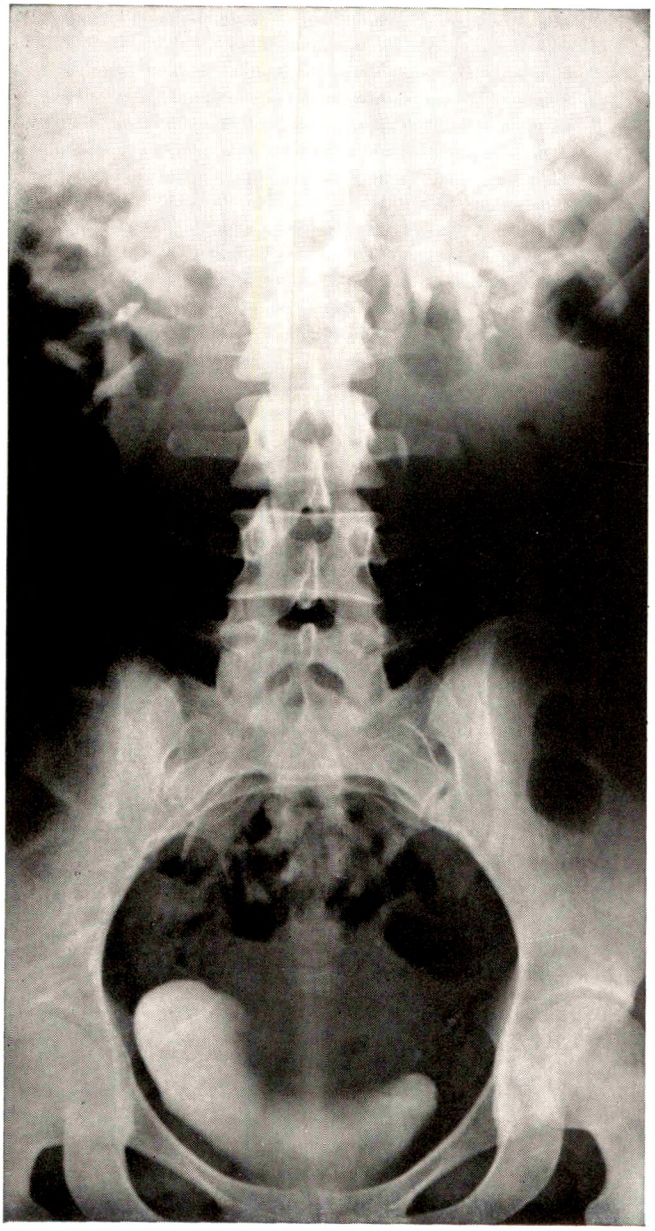
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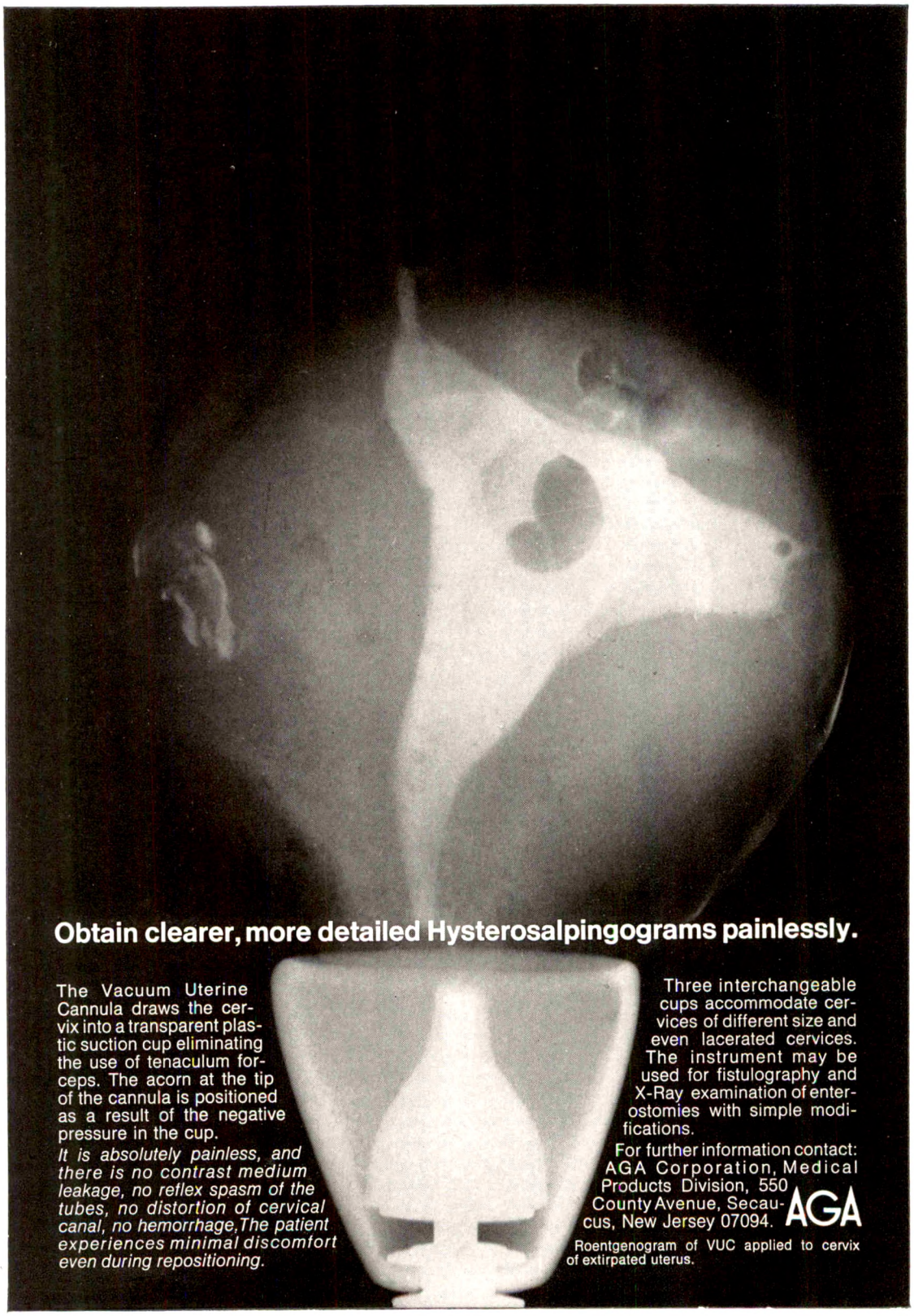


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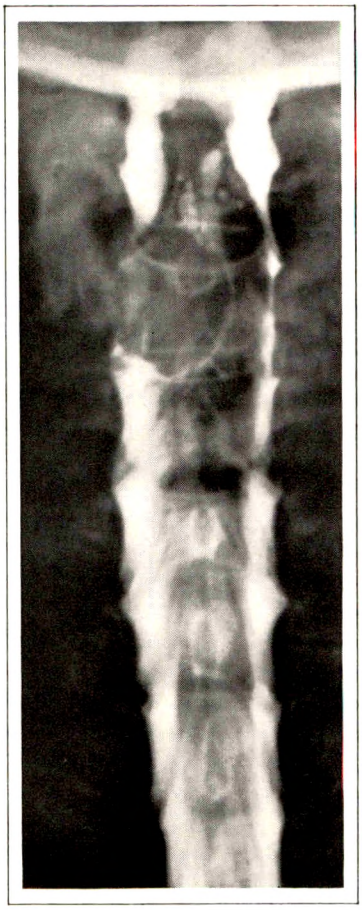
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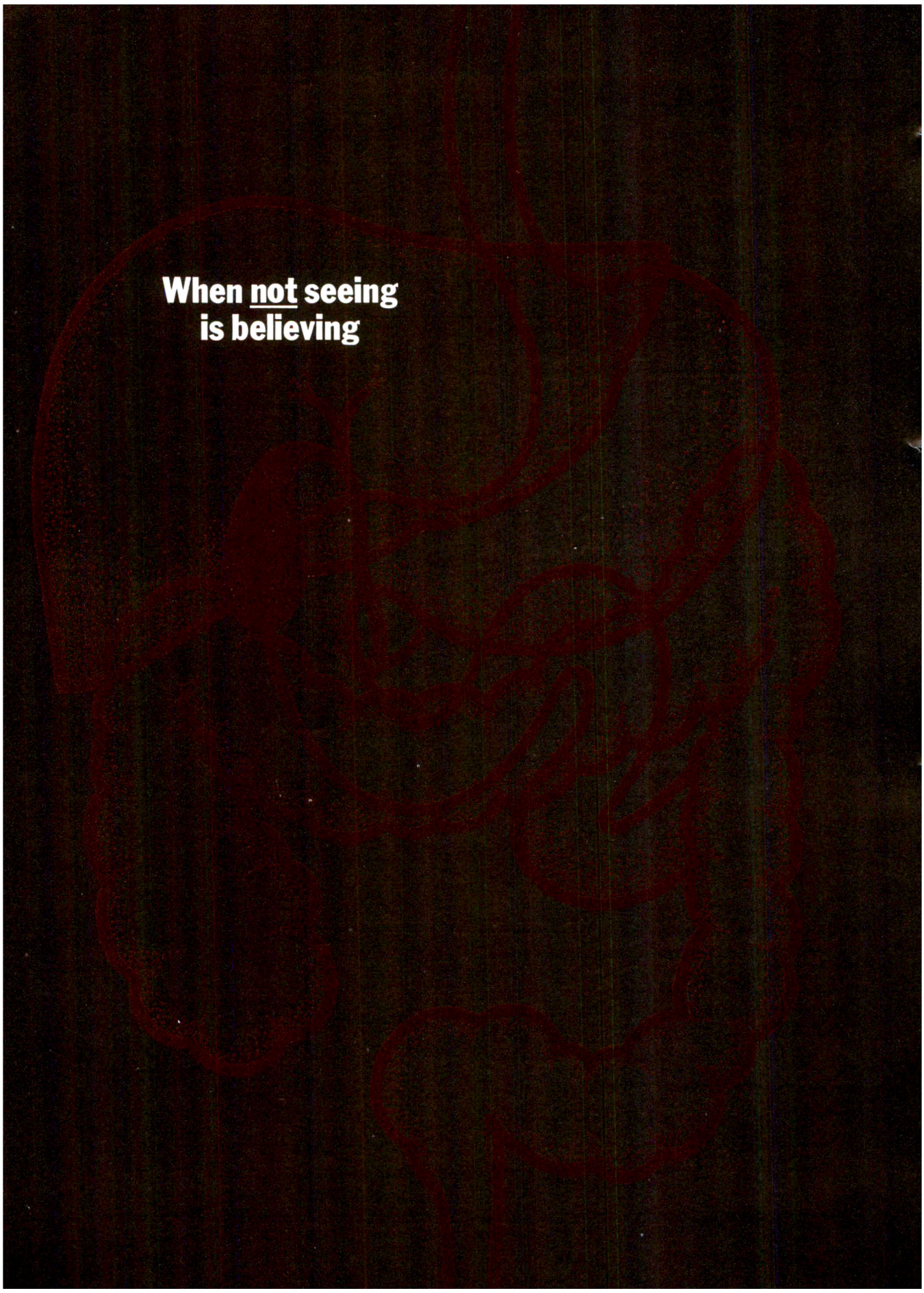
The tumor was excised following laminectomy of the third, fourth, and fifth vertebrae and the spinal cord was thoroughly decompressed. The patient did very well postoperatively and today is an essentially well woman.

Side Effects. Clinical reports indicate that the incidence and the severity of the side effects following Pantopaque myelography with aspiration of the medium is but slightly greater than with ordinary lumbar puncture. In 10-30 percent of such cases there may be transient symptomatic reactions consisting of slight temperature elevation and increase of symptoms referable to a back condition. When the medium is not removed, similar transient side effects occur with a slight elevation of temperature in a greater percent of patients. To reduce the reactions to a minimum and to facilitate the absorption of the medium, the bulk of the Pantopaque should be removed by aspiration after myelography.

Contraindications. Pantopaque should not be injected where a lumbar puncture is contraindicated, nor within 10 days of a previous lumbar puncture. The latter precaution is necessary to avoid subdural and extra-arachnoid extravasation. An injection should not be carried out until the operator is certain that his needle is in the subarachnoid space.

Limitations. Pantopaque has not been studied adequately from a clinical standpoint as a contrast medium for body cavities other than the subarachnoid space. The limitations and contraindications in other areas are not known.

Pantopaque, the trademark under which all leading x-ray dealers supply the compound ethyl iodophenylundecylate, is prepared as the myelographic contrast medium Iophendylate Injection, U.S.P. by Lafayette Pharmacal Inc., Lafayette, Indiana 47904. *Pantopaque is a registered trademark of Eastman Kodak Company.*


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Adverse Reactions: Most reactions are mild and transitory; serious side effects are very rare. Gastrointestinal effects (diarrhea, cramps, nausea, vomiting) are the most common. Usually the diarrhea consists merely of a few loose stools, although in isolated cases it may be severe. A mild stinging sensation during urination may occur, and rarely, skin rash, urticaria, pruritus, and flushing. One case of thrombocytopenia has been reported in a patient with a history of conjunctival hemorrhages. Subjective complaints have been: dryness of throat, burning on swallowing, heartburn, sore throat, dizziness, and headache.

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*Baker, H. L., Jr., and Hodgson, J. R. (Mayo Clinic and Mayo Foundation): Further studies on the accuracy of oral cholecystography, *Radiology* 74:239, Feb., 1960.

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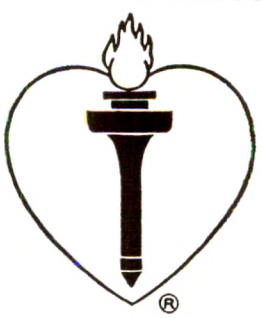
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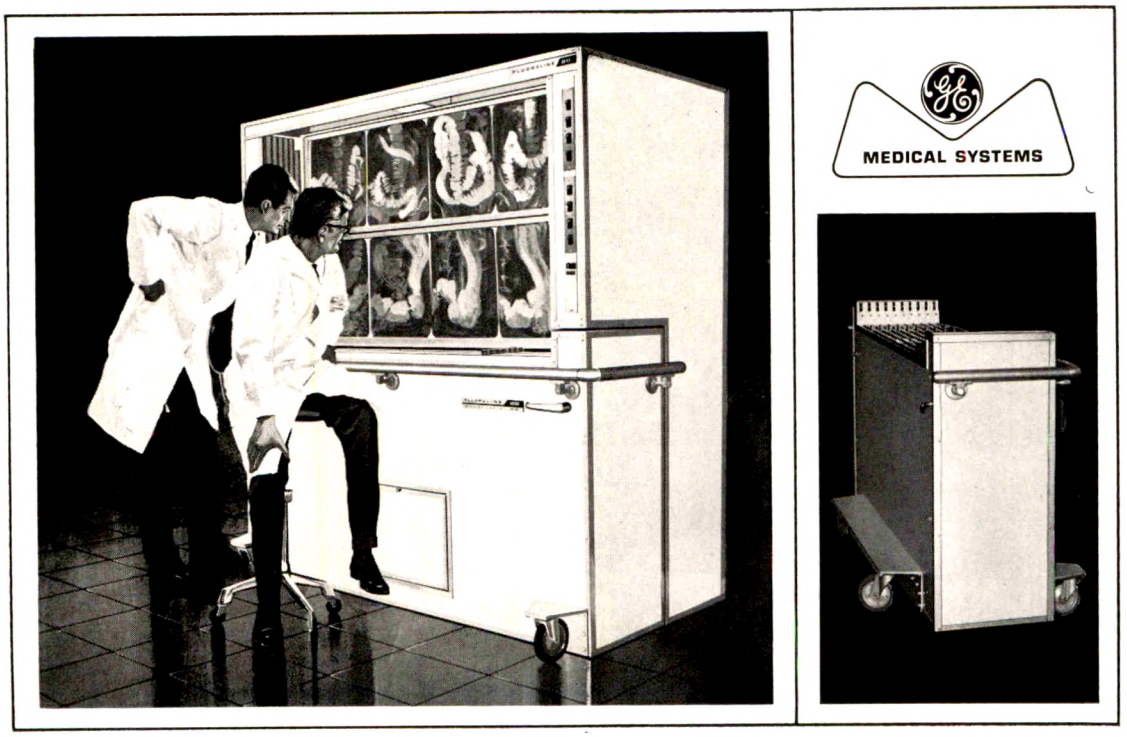


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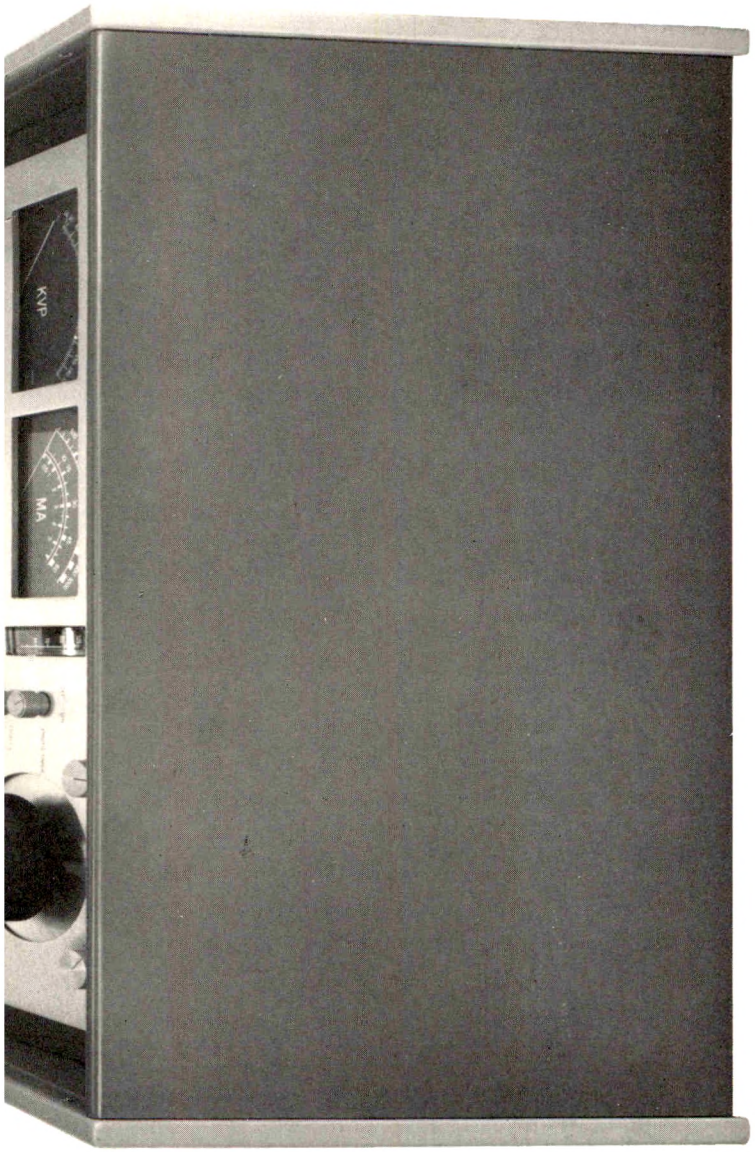
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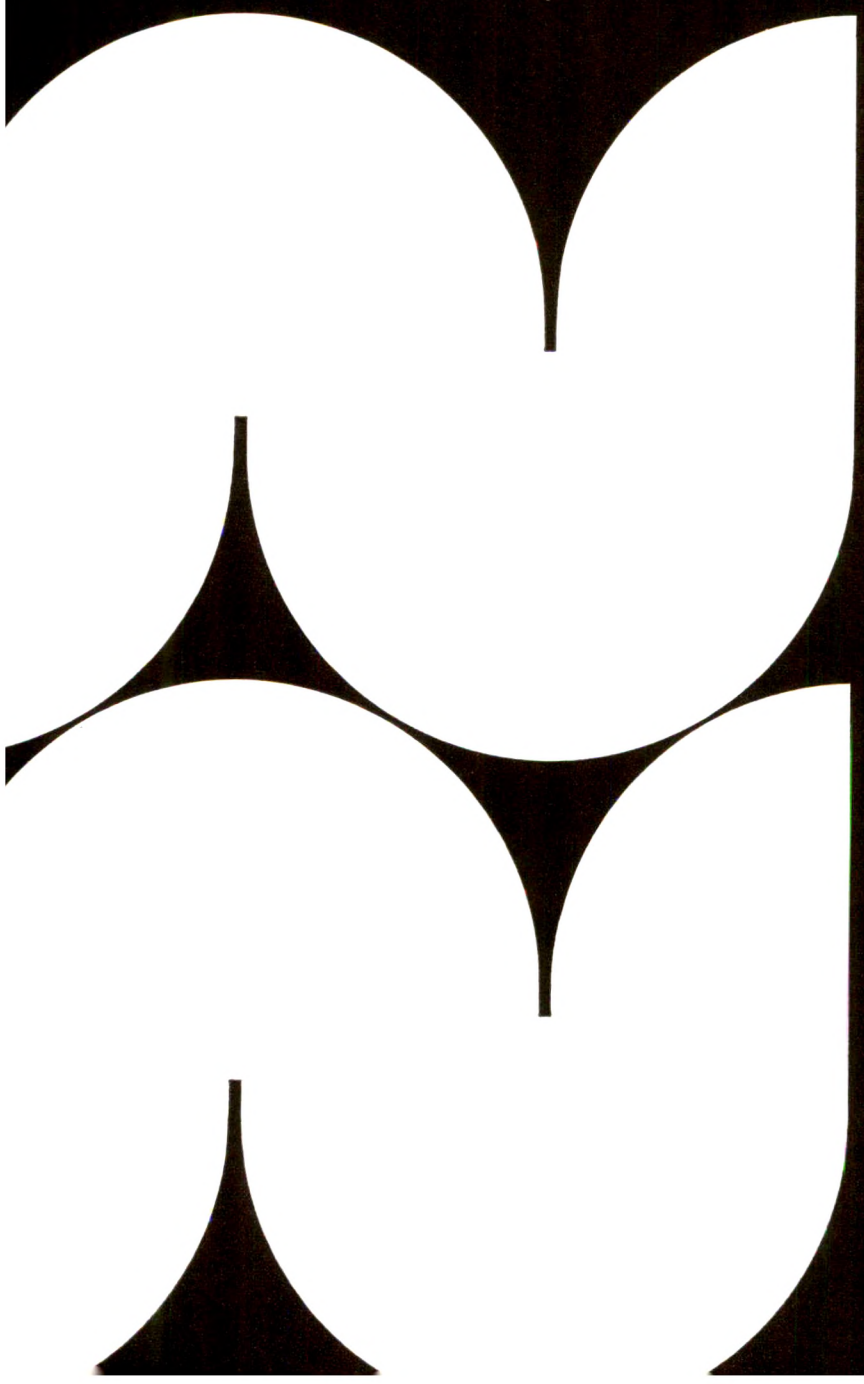
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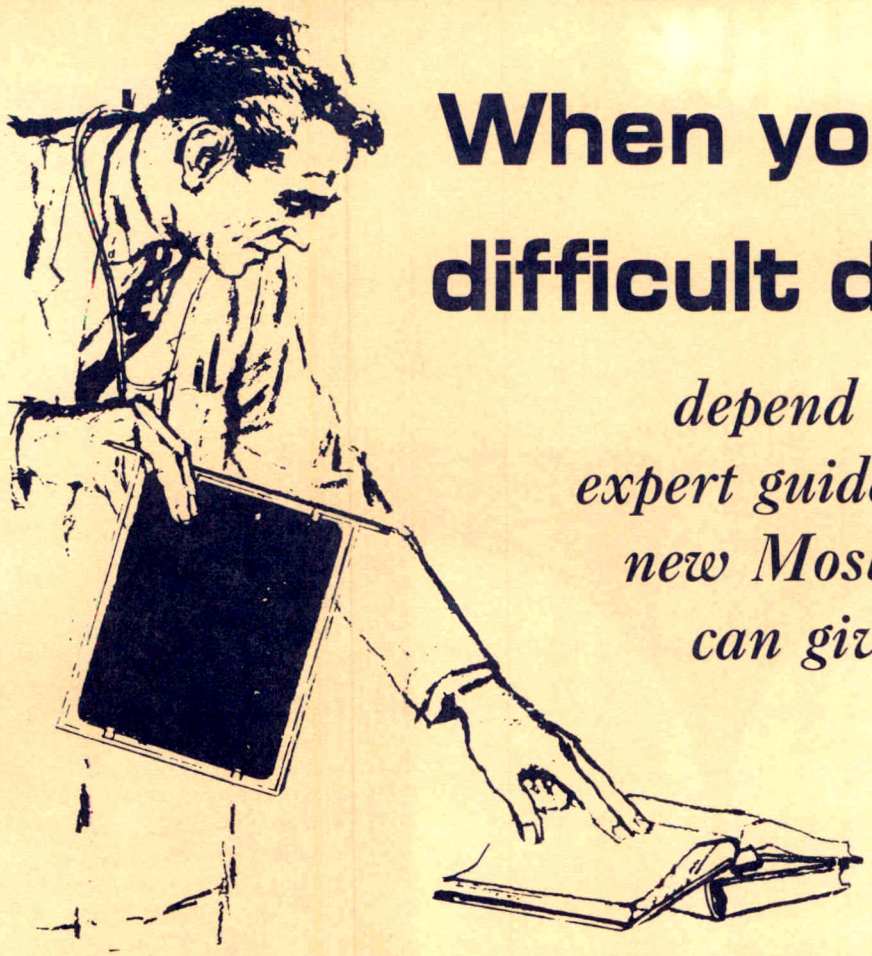
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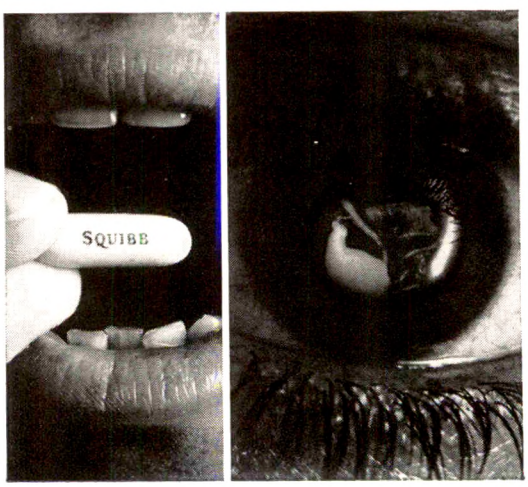
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For summary of contraindications, precautions, and side effects, see next page.



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References: 1. McLuhan, M.: Understanding Media: The Extensions of Man, New York, McGraw-Hill Book Company, 1966. **2.** Sanen, F. J.: Amer. J. Roentgen. *88*:797 (Oct.) 1962. **3.** Glenn, J. C., Jr., and O'Brien, P. S.: Southern Med. J. *56*:167 (Feb.) 1963. **4.** White, W. W., and Fischer, H. W.: Amer. J. Roentgen. *87*:745 (April) 1962. **5.** Juhl, J. H., *et al.*: Radiology *80*:87 (Jan.) 1963. **6.** Lewitan, A., and Garcia, J. F.: Amer. J. Dig. Dis. *10*:219 (March) 1965. **7.** McCrory, E.: J. Tenn. Med. Ass. *58*:258 (Aug.) 1965. **8.** Root, H.: Amer. J. Roentgen. *101*: 621 (Nov.) 1967. **9.** Crummy, A. B.: Wisconsin Med. J. *65*:84 (Feb.) 1966. **10.** Saltzman, G. F.: Acta Radiol. *54*: 417, 1960. **11.** Ludin, H., and Lauchenauer, C.: Schweiz. Med. Wochenschr. *90*:471, 1960.

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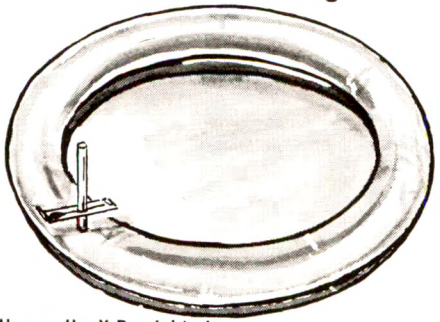
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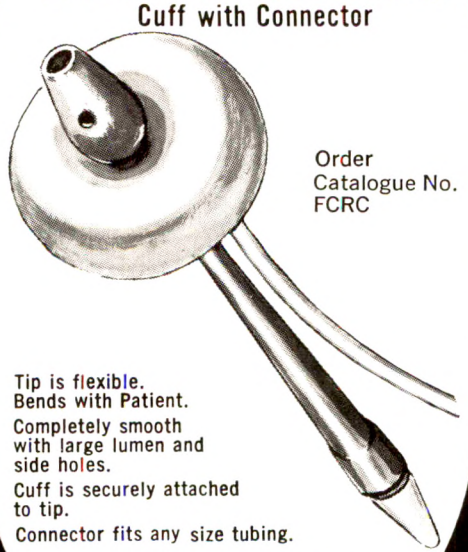
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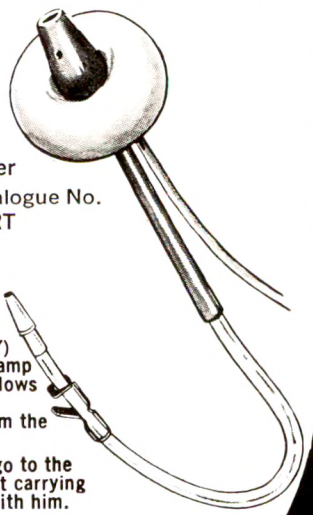
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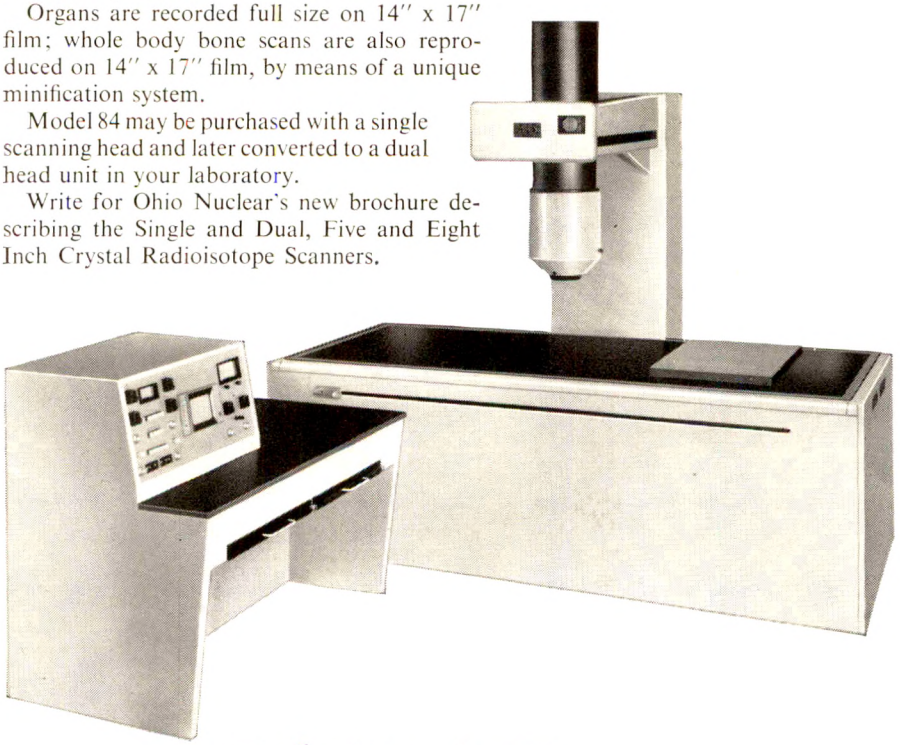
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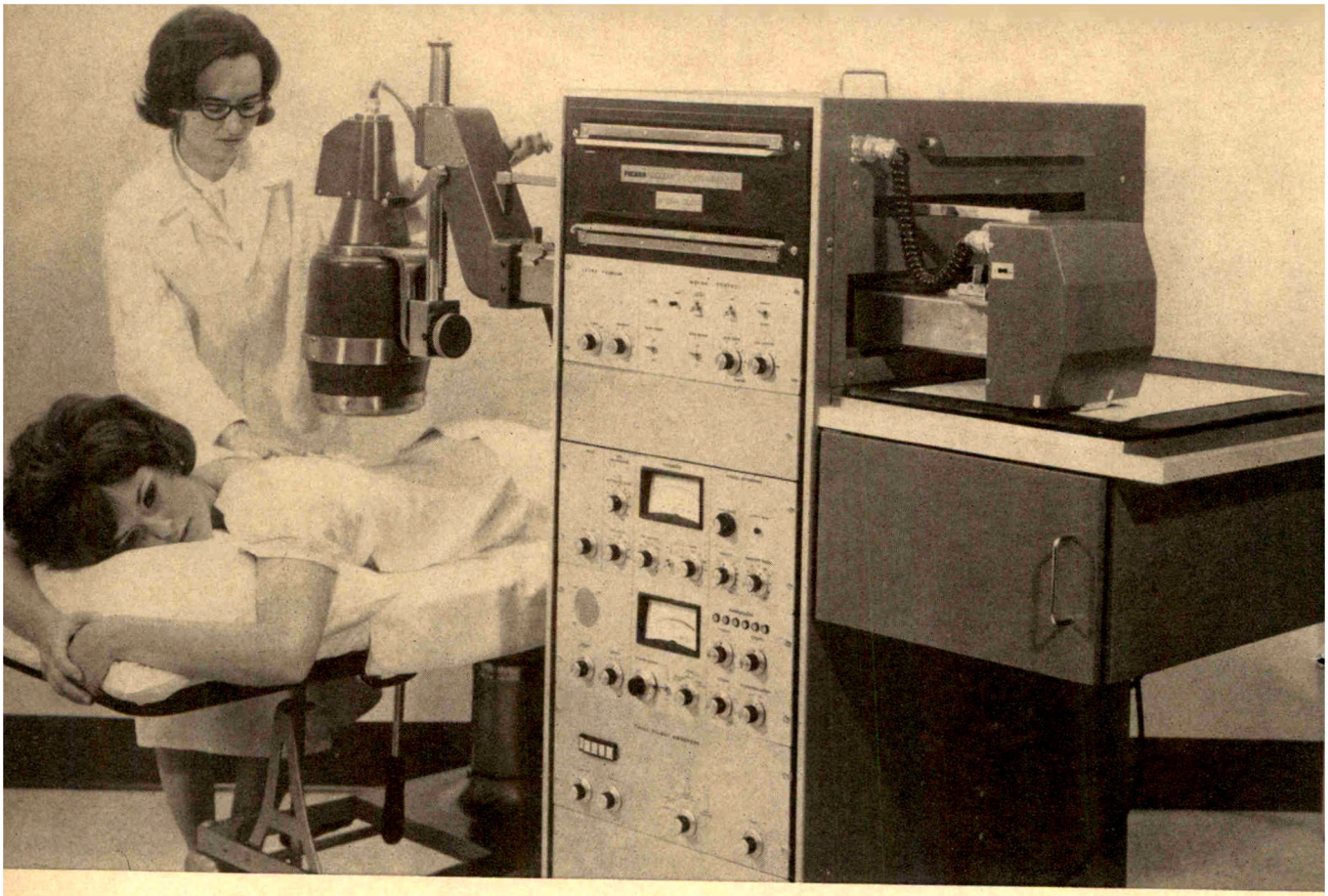
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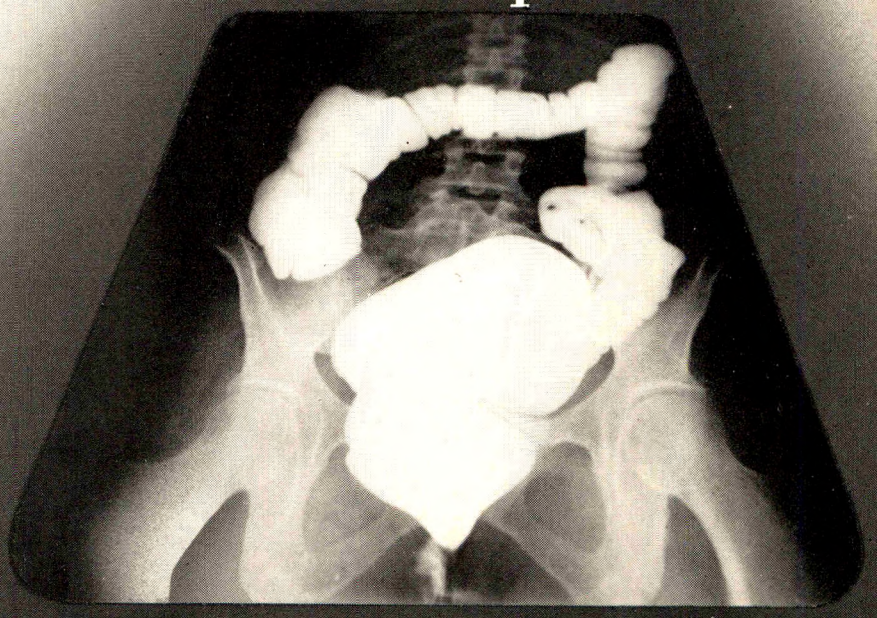
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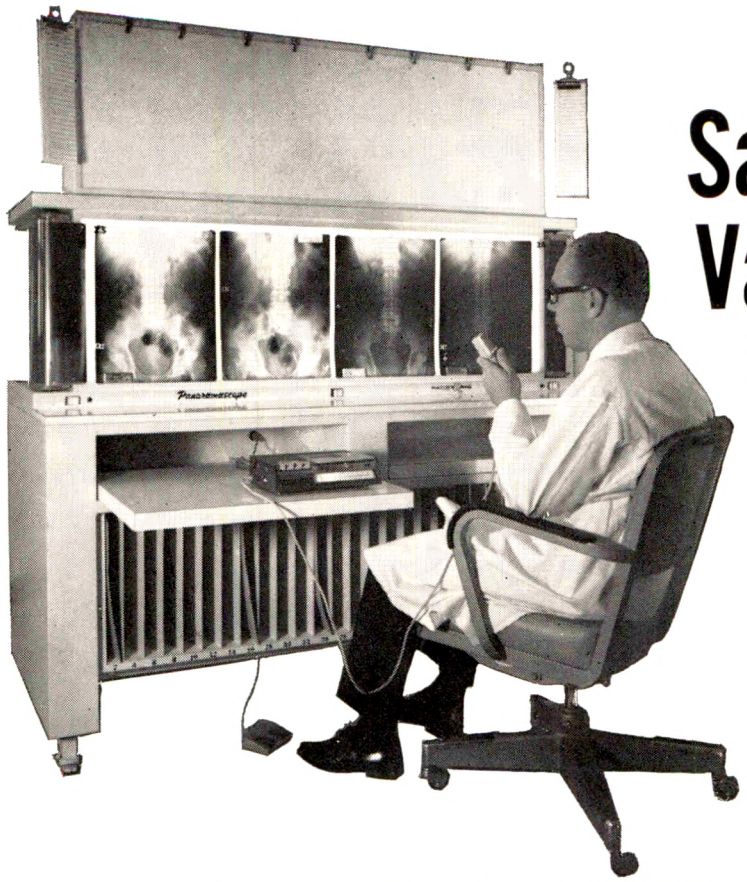
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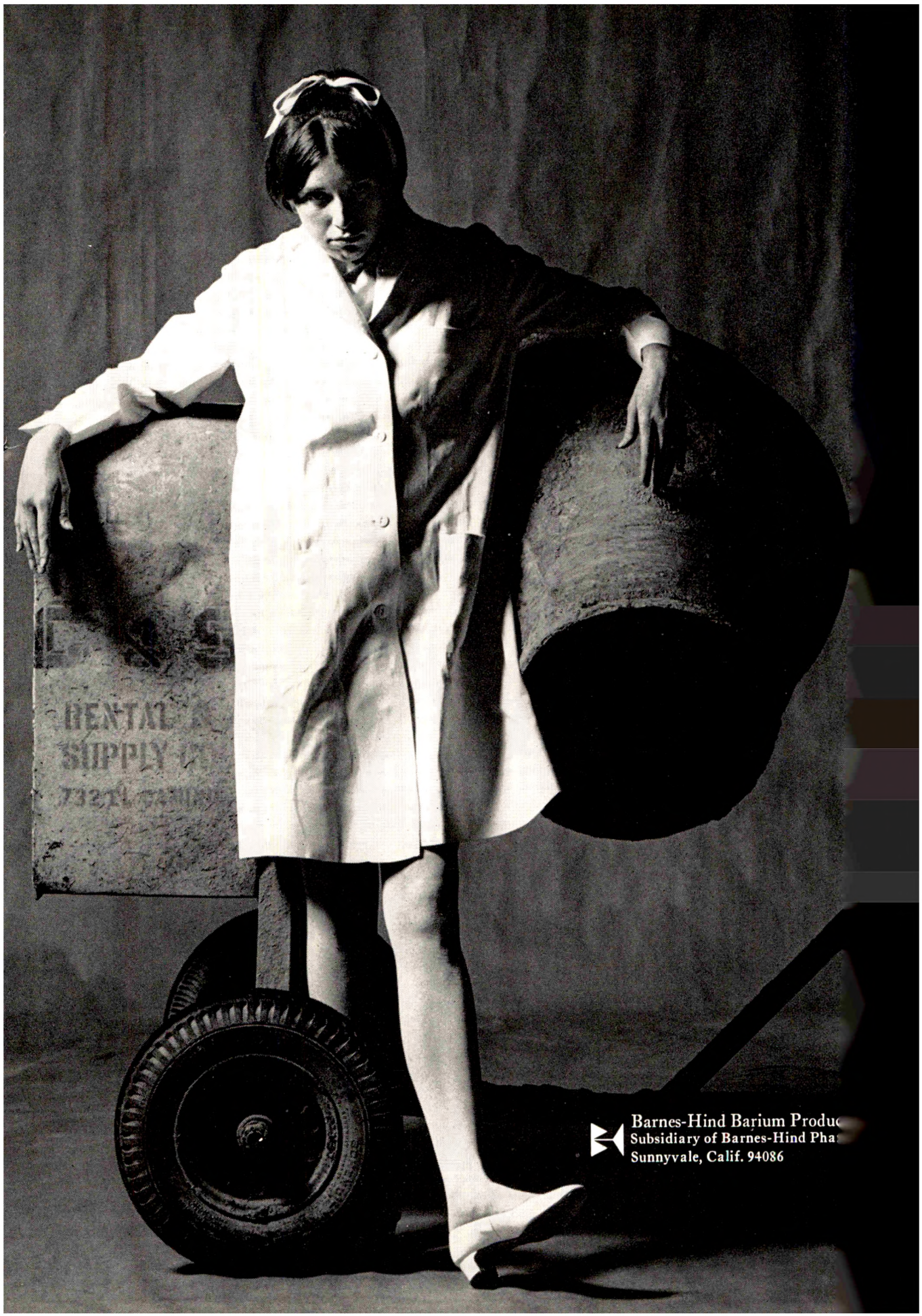
So why mix your own?

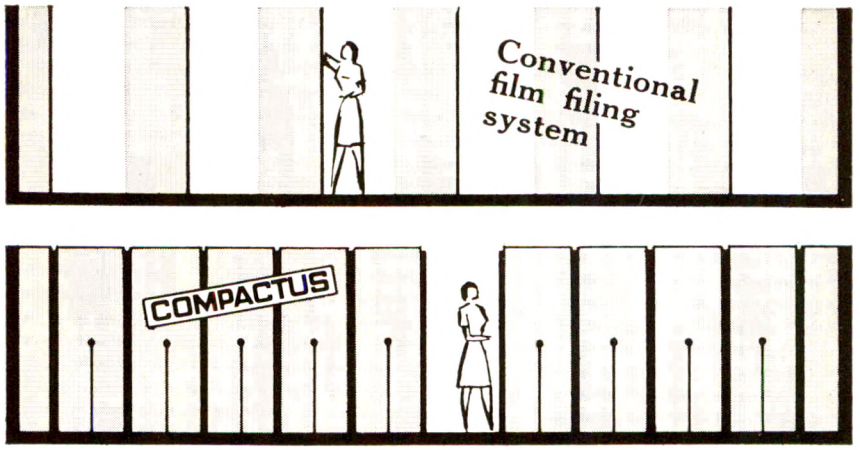
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(barium sulfate)

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Recommended dose: 1 tablespoonful "chewed" thoroughly before swallowing. Repeat with a second tablespoonful to ensure prolonged adherence and coating of the esophageal mucosa.


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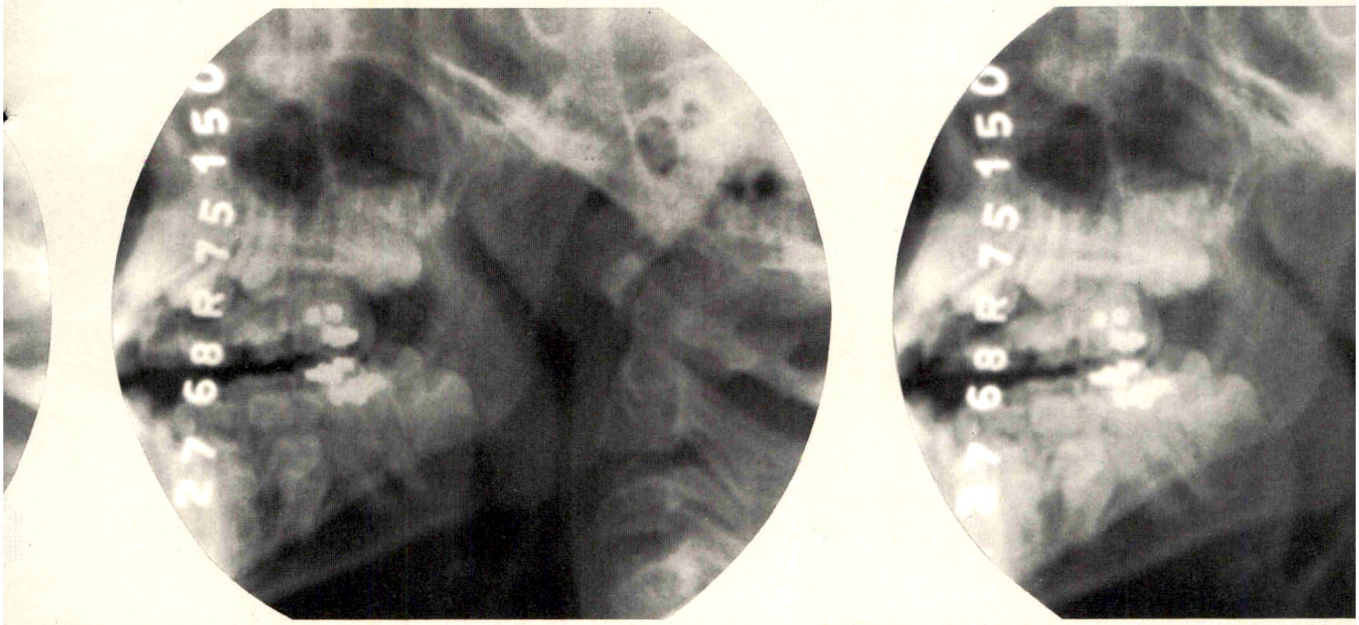
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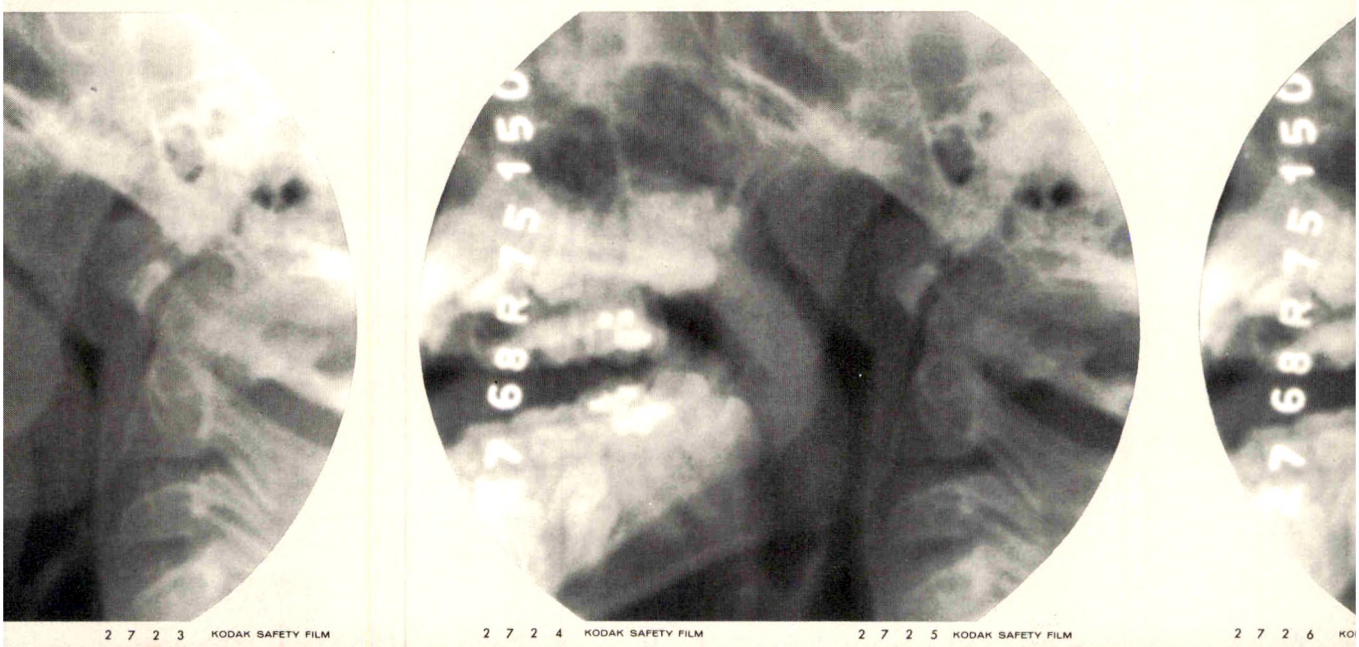
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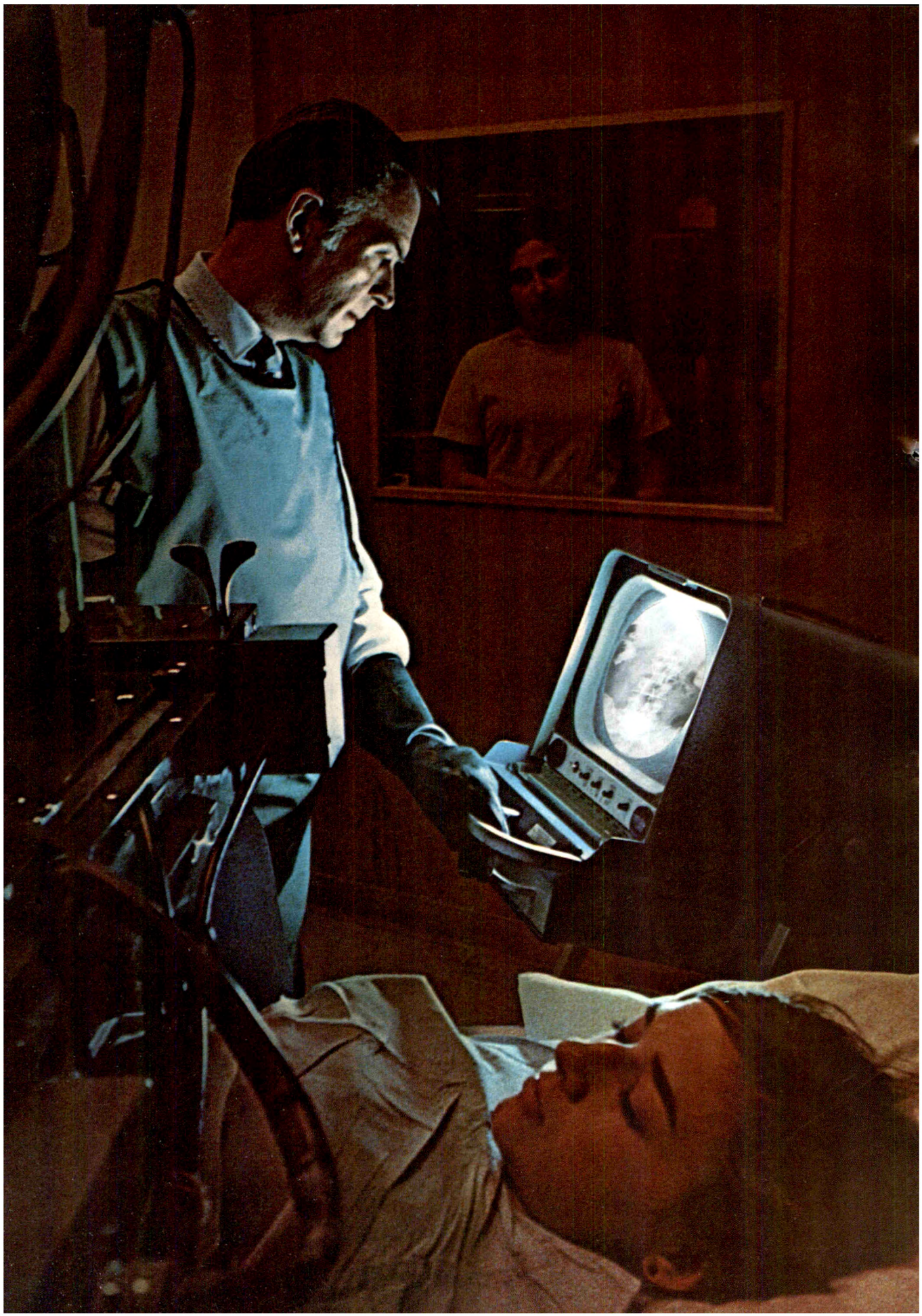
Kodak

90-second proof





New KODAK *RP* X-OMAT FLUROSPOT Film. 90-second processable. More on next page.



KODAK *RP** X-OMAT Films give more information, time after time.

Quality is the reason you get radiographs with more information when you use KODAK *RP* X-OMAT Films, Chemicals, Processor.

And film choice is an important part of Kodak quality.

Now there is a fourth 90-second film: the new KODAK *RP* X-OMAT FLUROSPOT Film (ESTAR-AH Base) represented here. The addition of this new special-purpose film, in 70mm and 3½-inch widths, to the three basic films—KODAK *RP*, *RP/L* and *RP/S* X-OMAT—gives you even greater flexibility to meet your requirements.

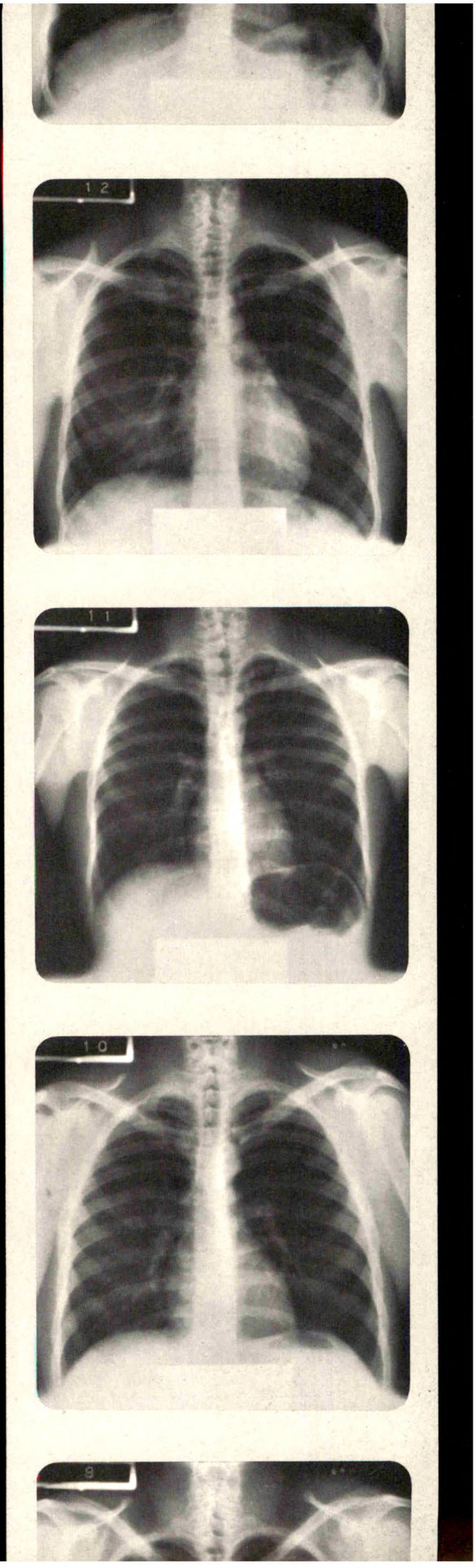
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Kodak

*Rapid Processing

EASTMAN KODAK COMPANY
Radiography Markets Division, Rochester, N.Y.



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For new hospital with 125 beds, 4 megavoltage machines, and a well equipped isotope-laboratory, is required fully licensed

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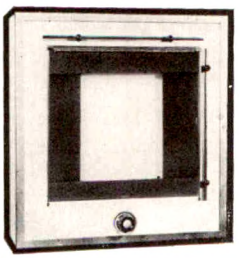
with scientific interests.

The hospital is one of the two main cancer-centers in Holland.

Possibilities for research work are given. Cooperation with the new medical faculty of Rotterdam is being arranged.

Applications with full particulars and salary requested to Dr. G. Schalij, medical director of the Rotterdam Radio-Therapeutic Institute, Groene Hilledijk 297, Rotterdam, Holland.

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INTENSIVE INSPECTION "CURTAINED" ILLUMINATOR: 17x17 in. viewing area with stepless brightness control providing all-over selective collimation down to point size. Distortion-free magnification by powerful two-lens aplanatic optics, weightlessly suspended in front of illuminator . . . (optional, not shown in picture).



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Telepaque®

brand of **iopanoic acid**

Contraindications: Contraindicated in advanced hepatorenal disease or severe impairment of renal function, severe gastrointestinal disorders that prevent absorption, and in patients sensitive to iodine compounds.

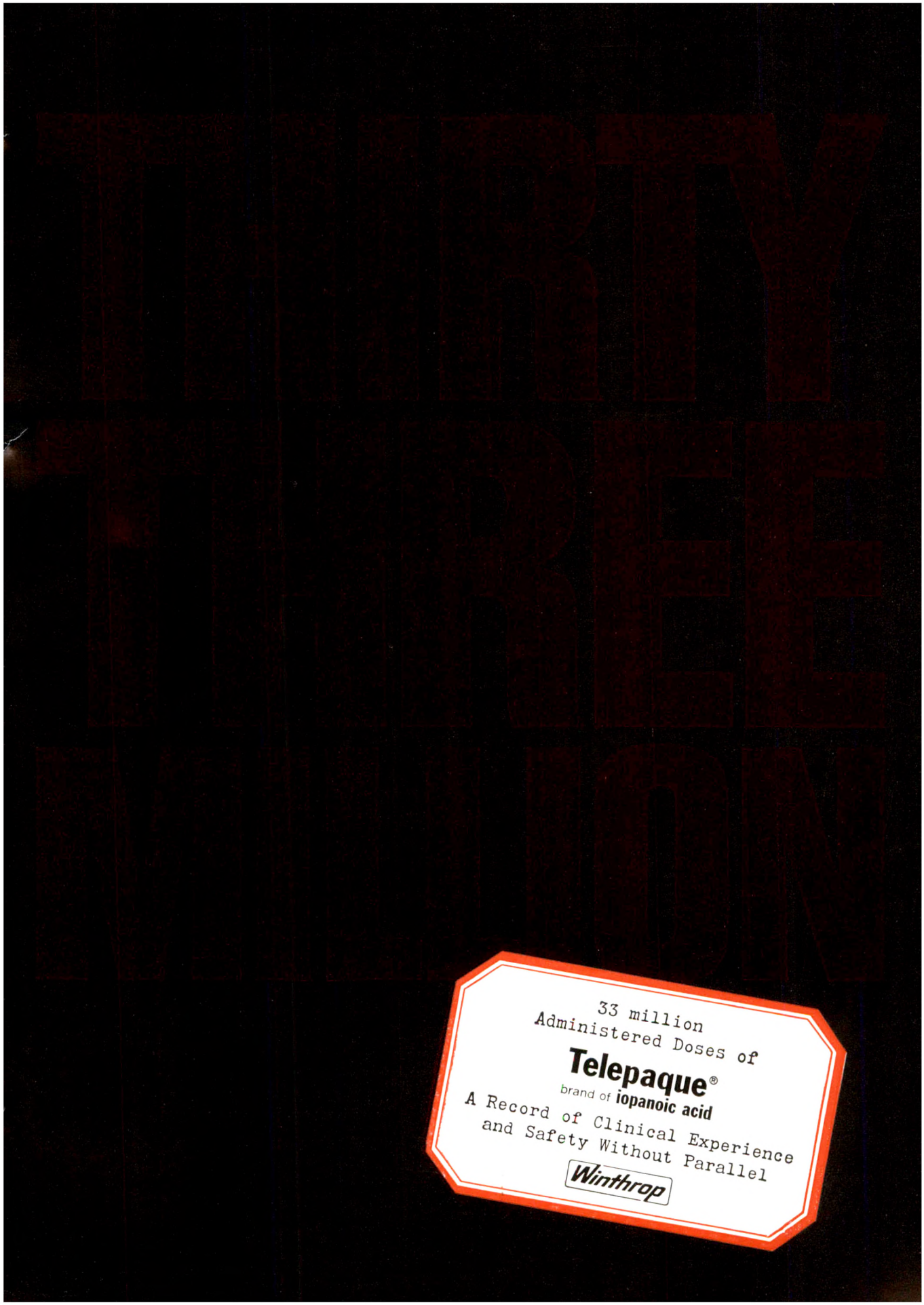
Precautions: Severe, advanced liver disease may interfere with metabolism of Telepaque, thus increasing the excretory load on the kidneys. Although renal difficulty has rarely been attributed to Telepaque, renal function should be assessed before cholecystography in severe, advanced liver disease, and renal output and hepatic function should be observed for a few days after the procedure. Patients with preexisting renal disease should not receive high doses of cholecystographic media. Possible renal irritation in susceptible individuals could result in reflex vascular spasm with partial or complete renal shutdown. Caution is advised in patients with coronary disorders, especially those with recent symptoms of coronary artery disease. Blood pressure should be observed after administration of cholecystographic media to these patients. Elevation of protein-bound iodine for several months and false positive urine albumin tests (for three days) may occur after ingestion of iodine-containing cholecystographic media.

Adverse Reactions: Most reactions are mild and transitory; serious side effects are infrequent. Gastrointestinal effects (diarrhea, cramps, nausea, vomiting) are the most common. Usually the diarrhea consists merely of a few loose stools, although in isolated cases it may be severe. A mild stinging sensation during urination may occur, and rarely, skin rash, urticaria, pruritus, and flushing. One case of thrombocytopenia has been reported in a patient with a history of conjunctival hemorrhages. Subjective complaints have been: dryness of throat, burning on swallowing, heartburn, sore throat, dizziness, and headache.

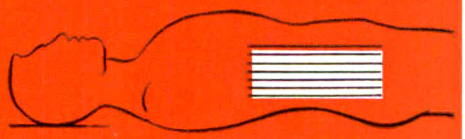
Usual Dosage: 3 Gm. (6 tablets) at night after a light supper.

Supplied: Tablets of 500 mg., envelopes of 6 tablets, boxes of 5 and 25 envelopes; also bottles of 500.

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Telepaque®
brand of iopanoic acid
A Record of Clinical Experience
and Safety Without Parallel
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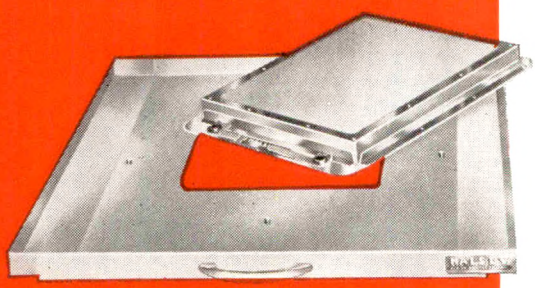
for body section radiography...



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Multi-Sette Jr. "3-5"

3 or 5 films at a single exposure



Multi-Sette Jr. "3-5"

Utilizes a special book of matched screens of different speeds to provide comparable density and detail in each of the films.

The 3-film model has 1 cm spacing between adjacent films; the 5-film model, ½ cm spacing.

Fits the conventional Bucky without requiring modifications, by means of the special adapter tray supplied. Precision-built, with stainless steel frame, aluminum door and magnesium front. Opens and shuts easily.

Available in a full range of sizes with DuPont or Radelin screen book. The 3-film and 5-film books are interchangeable.

Multi-Sette "7"

7 films at a single exposure



Multi-Sette "7"

For use with open table only

Can be installed in the Bucky housing after a modification (which does not interfere with conventional use). Spacing between adjacent films is 1 cm.

Available in a full range of sizes, with DuPont or Radelin screen book.

Multi-Sette Plesiosette "4"

4 films at a single exposure



Multi-Sette Plesiosette "4"

For close-section radiography

Has the same outside dimensions as conventional cassettes, so no adapter tray or Bucky modification is required. Spacing between adjacent films is 1 mm.

Available in 8 x 10″ and 10 x 12″ sizes, with Radelin PLT screen book.

Write for detailed literature

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SQUIBB

a research concept in contrast visualization

for clear definition of disease:

this oral medium is the message . . .

Oragrafin® Calcium (Squibb Calcium Ipodate) visualizes the gallbladder and ducts quickly and clearly with few undesirable reactions. For rapid or routine studies of the gallbladder and biliary ducts, Oragrafin permits efficient absorption for maximum concentration and excellent contrast—with bowel residue in only a small percentage of patients and few patient problems.

Oragrafin (Squibb Ipodate) in radiography — an advanced medium of biomedical communication. According to McLuhan's[1] provocative new theories of communications, all media are considered "extensions of man"—the means by which he extends his understanding and control of the universe and himself. In biomedical communications, where man monitors the diverse processes of molecular and cellular change, modern contrast radiography is an advanced medium.

Today, in cholangiography and cholecystography, as the medium becomes increasingly oral, the diagnostic message is clear, rapid, and convenient with Oragrafin (Squibb Ipodate).

For summary of contraindications, precautions, and side effects, see end of this advertisement.



the medium:

Oragrafin®

Squibb Ipodate

the message:

maximum concentration... excellent toleration

high absorption index—"No one will dispute the statement that the diagnostic reliability of oral cholecystography depends upon the degree of absorption of the contrast medium employed."[2] Radioisotope studies with ipodate sodium show a markedly improved absorption index (approximately 70 per cent) with no increase in the toxic properties.[2]

excellent opacification—"In addition to its ease of administration and safety, its principal advantages are a high yield of diagnostic films...."[3]

less bowel residue—"Incomplete and variable absorption of a cholecystographic agent is not desirable, for the opacification of the gallbladder is then less dependent on the status of the gallbladder and more a reflection of the percentage absorption."[4]

"Opaque material in the bowel was found in 46 per cent of [105 patients in] the...[iopanoic acid] group as compared with 9 per cent of those [99] of the [Oragrafin Sodium Capsules]...group."[4] In another study, 49 of 100 patients receiving iopanoic acid had residue in the gastrointestinal tract, while only 15 of 100 patients receiving Oragrafin Sodium Capsules had such residue.[5]

no evidence of nephrotoxicity, infrequent side effects—In contrast to findings with other cholecystographic agents, Lewitan and Garcia[6] reported in their 246-patient study: "With ipodate calcium... there was no clinical evidence of immediate or delayed nephrotoxicity in any of the patients given it...."[6] To study possible renal toxicity, "Creatinine clearance tests were also done before and after administration of multiple doses in excess of 6 gm. in 8 cases, and showed no significant alterations."[6] However, "Multiple doses beyond 6 gm. are not recommended."[6]

In their study of 120 patients, Glenn and O'Brien reported "...no reactions in this series of patients attributable to the administration of [Oragrafin]...."[3]

And, McCrory reported that Oragrafin Sodium and Calcium was "...used routinely in cholecystographic studies in approximately 2000 patients with excellent diagnostic films and only rare and mild reactions."[7]

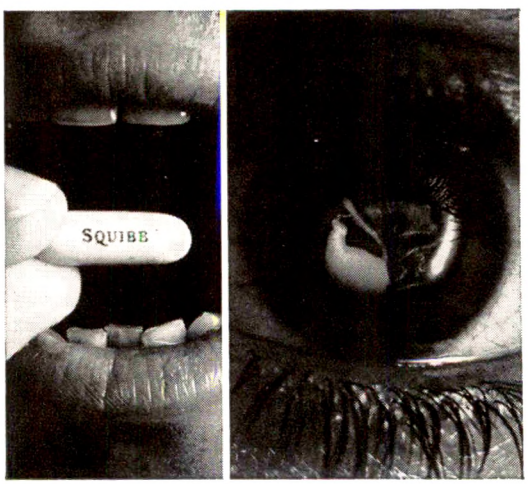
fewer side effects than iopanoic acid—According to White and Fischer,[4] 36 (36.4%) instances of side effects occurred in 99 cases with Oragrafin Sodium, 3 Gm. compared with 87 (82.9%) in 105 cases with iopanoic acid, 3 Gm. Kinds of side effects noted were nausea, vomiting, diarrhea, cramps and dysuria—all less frequent with Oragrafin Sodium (Squibb Sodium Ipodate).

Juhl,[5] in his study of 200 patients (100 on iopanoic acid and 100 on sodium ipodate), found that the incidence of nausea and vomiting was equal in the two groups.[5]

Oragrafin (Squibb Ipodate) dosage schedules
Oragrafin (calcium or sodium ipodate) permits overnight cholecystography and cholangiography.

	Gallbladder Films		Films of the Gallbladder and Biliary Ducts
11 P.M.	6 Capsules OR (or 12 Capsules)	1 packet of Granules (or 2 packets)	6 Capsules (or 1 packet of Granules, if preferred) and
next morning 8 A.M.			1 packet of Granules
9 A.M.	Visualization of gallbladder	Visualization of gallbladder	Visualization of ducts and gallbladder
10 A.M.			
11 A.M.			

For summary of contraindications, precautions, and side effects, see next page.



speed and convenience of Oragrafin® Calcium Granules

Squibb Calcium Ipodate

new clinical study[8] demonstrates improved diagnoses with calcium ipodate—"A group of 114 patients with poorly filled gallbladders after routine administration of iopanoic acid were given 6 gm. of [calcium] ipodate granules immediately following their routine cholecystography. In 66 per cent of these patients opacification of the gallbladders was obtained within 3 hours, allowing a definite diagnosis. Of the remaining 33 per cent, one-half were ultimately proven diseased." "It is apparent that many poorly visualized gallbladders can be rendered visible by the ingestion of ipodate granules.... A whole day may be saved and other diagnostic studies may be performed."[8]

patient convenience—Routine cholecystography night-before procedure is easy for patients to follow; palatable granules further enhance patient acceptability. Rapid clearance of medium permits same-day administration and gallbladder and ductal films, and if necessary, same-day re-examination; reduces need for I.V. studies.

rapid absorption permits same-day re-examination—To determine the cause of nonopacification after routine cholecystography using 6 capsules, physicians may require re-examination by repeating the procedure at a later date (sometimes doubling dose to 12 capsules), or by administering more agent the evening of the first unsuccessful examination (again sometimes doubling dose to 12 capsules), and repeating the study the next day. "The advantage of the calcium ipodate method is that the examination can be completed in five additional hours with a limited dose of contrast agent."[9]

"a valuable medium for peroral cholegraphy"[6]—Rapidly absorbed from the gastrointestinal tract, calcium ipodate has been reported by some investigators to be diagnostically superior to other oral cholangiographic contrast agents.[10,11] With careful timing of the examination and the use of tomograms or laminograms, the frequency of good results can approximate that obtained with intravenously administered agents.[10] According to Lewitan and Garcia,[6] the medium's relative safety makes it a valuable medium for peroral cholegraphy. Timesaving and economical Oragrafin Calcium Granules may be particularly useful in certain patients for whom I.V. radiography presents potential hazards, such as elderly patients and those with cardiovascular disease.

Unique among oral media, Oragrafin Calcium Granules permits same-day films of the gallbladder and the ductal system.

dosage schedule for films of gallbladder and ductal system

8 A.M.	2 packets of granules
9 A.M.	visualization of ducts
10 to 11 A.M.	visualization of gallbladder

Contraindications: Contraindicated for persons sensitive to oral iodine compounds or for patients with *combined* renal and hepatic disease or *severe* kidney impairment. Gastrointestinal disorders, which may interfere with absorption, or liver dysfunction, which may result in inadequate biliary secretion of medium, are likely to result in unsatisfactory visualization.

Precautions and Side Effects: Mild and transient nausea, vomiting, or diarrhea sometimes occur; but the incidence can be reduced by using the calcium granules and restricting the dosage to 3 Gm. Transient headache, dysuria, or abdominal pains may occur.

Hypersensitivity reactions may include urticaria, serum sickness-like reactions, and rarely anaphylactoid shock. They are more likely to occur in the individual with a history of allergy, asthma, hay fever, or urticaria and in the individual who is known to be hypersensitive to iodine compounds. Antihistamines and corticosteroids are used to control hypersensitivity reactions; but the occasional serious anaphylactoid reactions require the immediate use of epinephrine or phenylephrine, oxygen, and intravenous corticosteroids.

For full information see Package Insert.

Supply: The calcium salt (Oragrafin Calcium Granules) is available in single-dose foil packets providing 3 Gm. of calcium ipodate as Granules dispersed in flavored sucrose. The sodium salt is available in capsule form (Oragrafin Sodium Capsules) providing 0.5 Gm. sodium ipodate per capsule.

References: 1. McLuhan, M.: Understanding Media: The Extensions of Man, New York, McGraw-Hill Book Company, 1966. **2.** Sanen, F. J.: Amer. J. Roentgen. *88*:797 (Oct.) 1962. **3.** Glenn, J. C., Jr., and O'Brien, P. S.: Southern Med. J. *56*:167 (Feb.) 1963. **4.** White, W. W., and Fischer, H. W.: Amer. J. Roentgen. *87*:745 (April) 1962. **5.** Juhl, J. H., *et al.*: Radiology *80*:87 (Jan.) 1963. **6.** Lewitan, A., and Garcia, J. F.: Amer. J. Dig. Dis. *10*:219 (March) 1965. **7.** McCrory, E.: J. Tenn. Med. Ass. *58*:258 (Aug.) 1965. **8.** Root, H.: Amer. J. Roentgen. *101*: 621 (Nov.) 1967. **9.** Crummy, A. B.: Wisconsin Med. J. *65*:84 (Feb.) 1966. **10.** Saltzman, G. F.: Acta Radiol. *54*: 417, 1960. **11.** Ludin, H., and Lauchenauer, C.: Schweiz. Med. Wochenschr. *90*:471, 1960.

for clear definition of disease: in oral cholangiography and cholecystography

Oragrafin®

Squibb Ipodate

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'The Priceless Ingredient' of every product is the honor and integrity of its maker.

A 2810

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All movements of HEAD, ARMS, COUCH and STRETCHER

now in the palm of your hand!



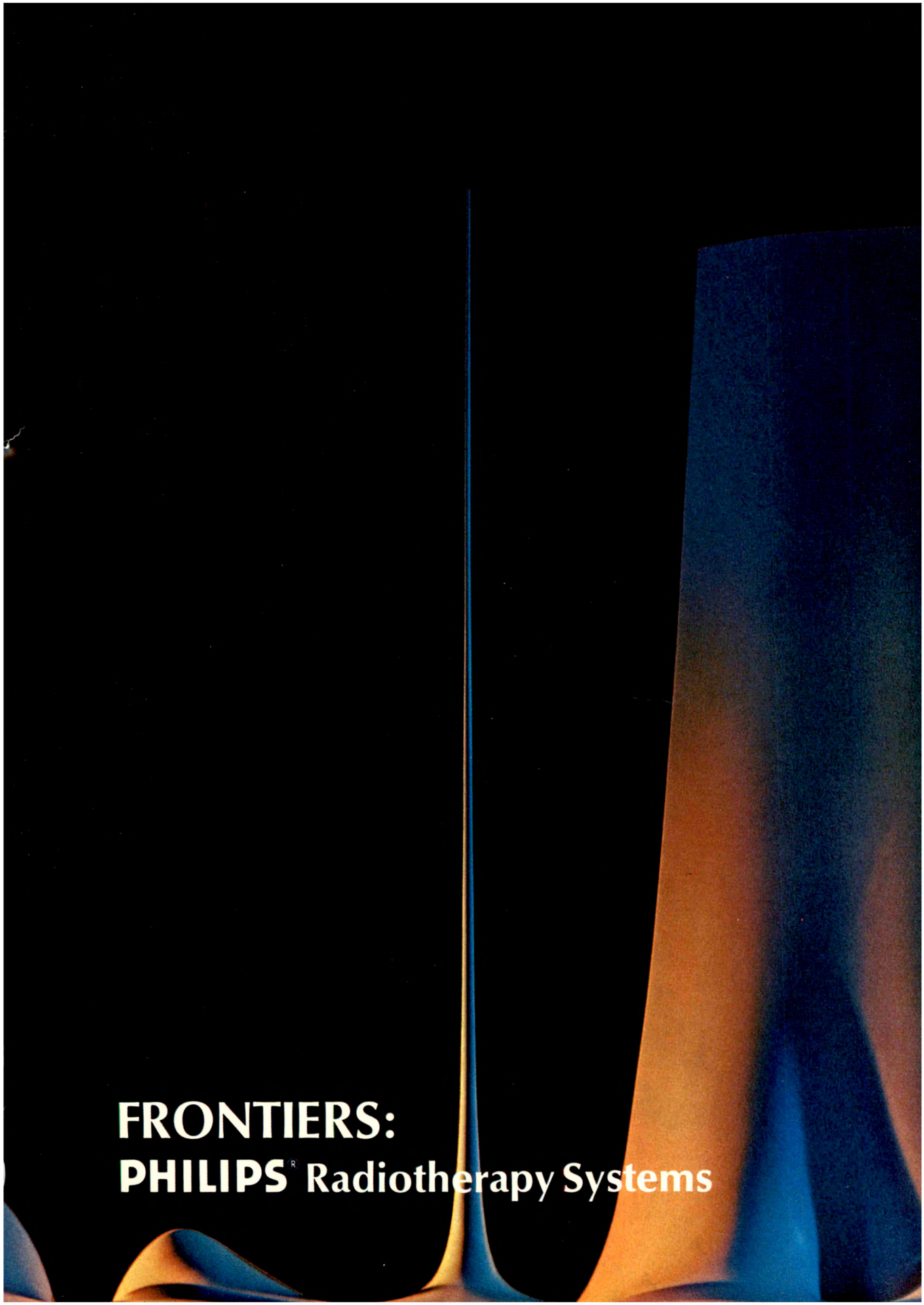
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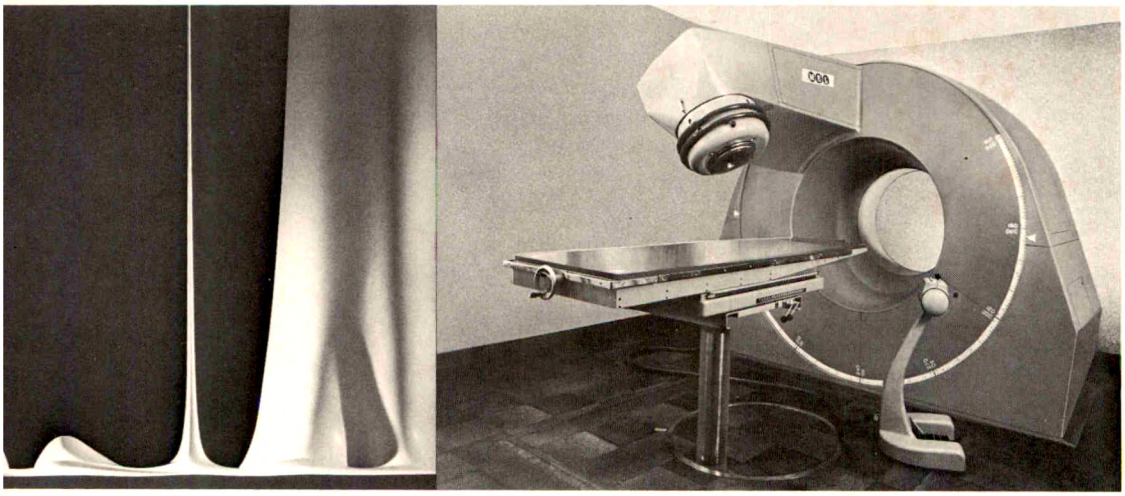


Photo by Erich Hartmann, Magnum Photos

Megavoltage Linear Accelerator—X-ray and Electron Outputs

TOTAL SPECTRUM THERAPY SYSTEMS

The oldest, most respected name in radiation physics also deals in tomorrow's concepts. Radiation physicists and therapists throughout the world use Philips Systems for treatment and research to expand the frontiers of radiotherapy. While our engineers continue to develop instrumentation which offers both simplicity and sophistication for tomorrow, we are ready for your needs today.

Whether your therapy department is new, expanding in size and services, or simply ready to replace equipment, we can offer you the widest scope and latest state-of the-art—from grenz to gamma rays.

We have therapy simulators, treatment tables, and complete accessories for techniques you now have, and many to help you explore new applications. And, these systems all offer more features for patient safety and comfort, more labor saving features, and more features to increase efficiency, and save you money and time.

New Hard Ray Equipment

We even have a breakthrough—a new hard ray, short range technique system that delivers 300kV, 6.8Cu HVL at 100 R/min! It's called the RT 305. It is small, powerful, and produces depth doses superior to conventional x-ray therapy units—approaching that of Cobalt 60. A 250kV version is also available.

Your Philips supplier can tell you more about these systems. Or, you can get in touch with the Medical Systems Division of North American Philips Corporation.

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MEDICAL SYSTEMS DIVISION

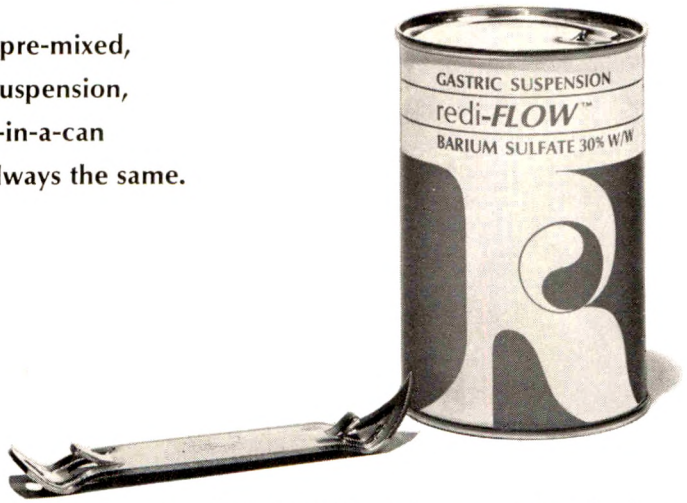
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M-59

No two ways about redi-FLOW™

(Gastric Suspension Barium Sulfate 30% w/w)

It's the pre-mixed,
stable suspension,
barium-in-a-can
that's always the same.



No two ways about **redi-FLOW™** (gastric suspension barium sulfate). It's always the same. Get the picture you want with the same patient at later dates because there is no variable factor in the mixing. **redi-FLOW™** (gastric suspension barium sulfate) is always ready-made to the same specifications of barium content, of specific gravity, of suspension, and of flow properties—day after day, month after month. It flows evenly as a consistent, uniform column of barium—doesn't precipitate in gastric fluid or small bowel. Your patients will love it. But don't let them have *all* the pleasure . . . try some yourself . . . it tastes like a good milkshake. No two ways about it—you'll like **redi-FLOW™** (barium sulfate suspension). Test it by using the coupon.

FLOW PHARMACEUTICALS, Inc.
Subsidiary of Flow Laboratories, Incorporated
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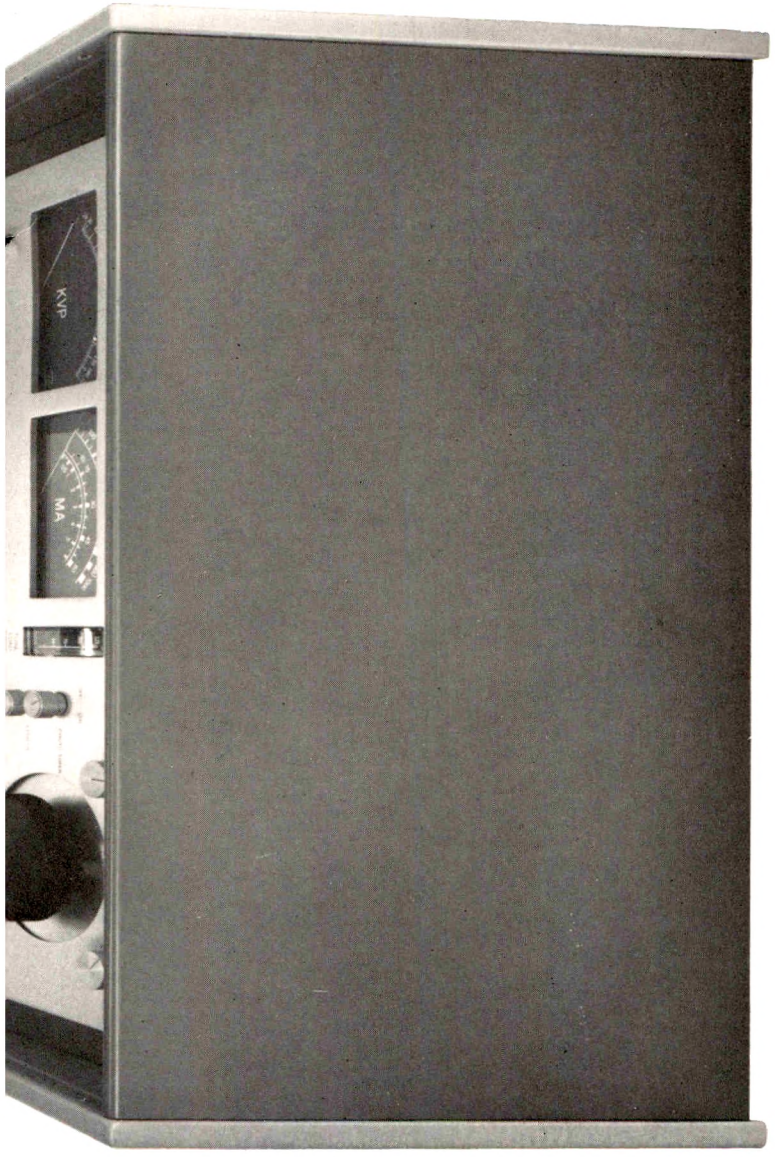
Send **redi-FLOW™** (gastric suspension barium sulfate , 30% w/w) samples to:

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City _____ State _____ Zip _____

Pick
your power:
1000 MA 3-phase,
2000 MA single-phase,
1600 MA 3-phase.



What do you look for in a high-power generator? Maybe the first thing should be an honest range of choice. And only one equipment manufacturer offers you that. For instance:

2000 MA single-phase with a revolutionary new x-ray tube that gives maximum power utilization.

1600 MA three-phase (twelve pulse) with up-to-the-minute flexibility and push-button simplicity.

And 1000 MA three-phase (twelve pulse) that gives you all that high power at a really sensible price.

Who's the manufacturer? The Profexray Division of Litton Medical Products, of course.

Talk over your high-power needs with a Profexray engineer. He's the only one who can let you pick exactly what you want.

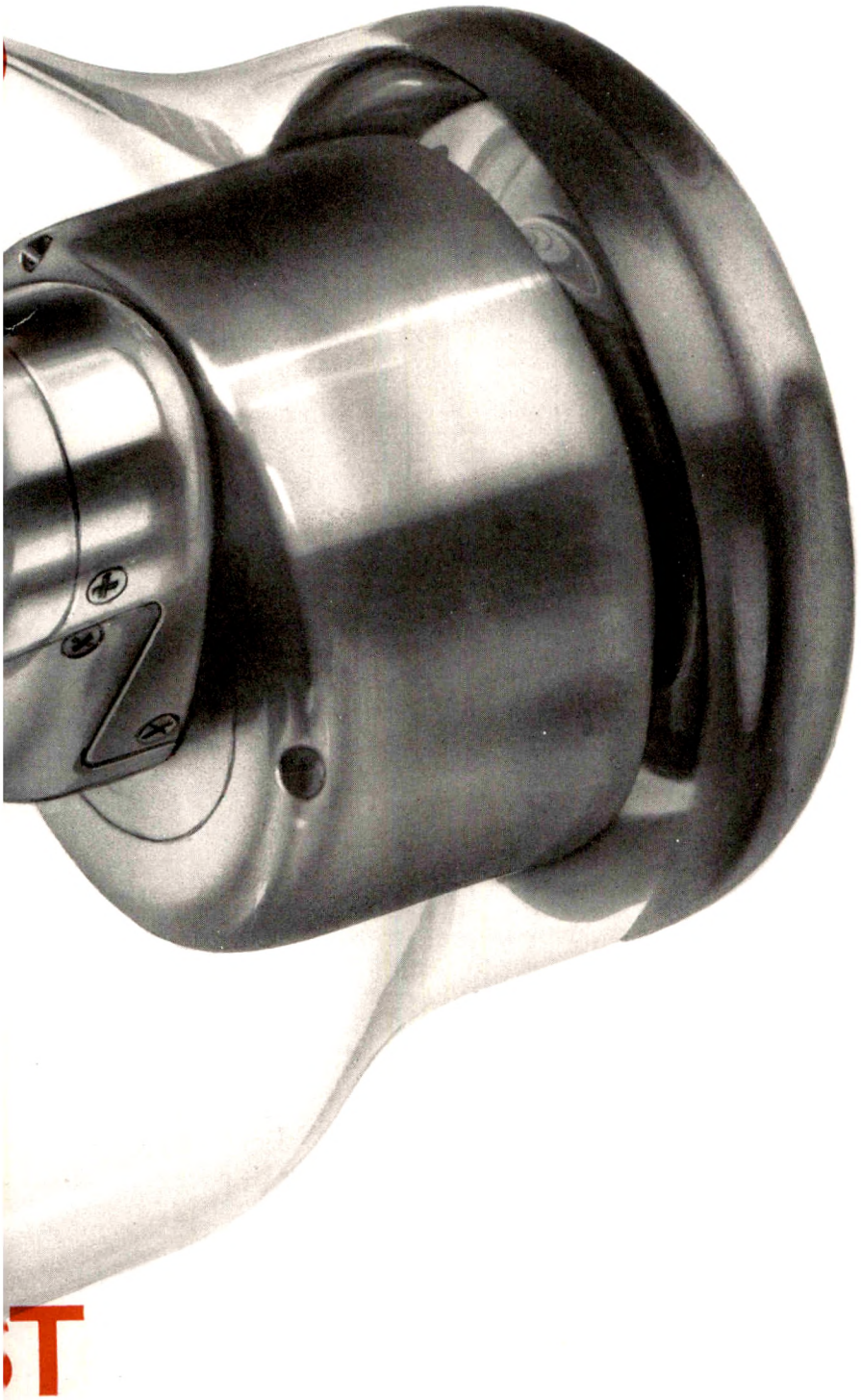
Instead of what he happens to be pushing.

Litton Medical Products
A Litton Industries Group, Profexray Division
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A NEW LINE OF HEAVY ROTATING ANODE X-RAY TUBES THAT LAST AND LAST

AND LAST AND LAST AND LAST

DUTY TUBES



the remarkable new DURATRONS by DUNLEE

Designed to fit most housings

Today's X-ray department. More traffic. More sophisticated. More exposures per hour. Someone had to develop an X-ray tube insert to meet the demands of today's radiology.

Dunlee did.

Superbly engineered, the Dunlee Duratron 175 and 140 rotating anode tubes have a high heat storage capacity, 175,000 H.U. on the 175 and 140,000 H.U. on the 140. Their high dissipation rate makes them applicable for all types of fluoroscopic, spot film and general radiographic service.

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Specify the X-ray tube insert designed for today's radiology. Duratron by Dunlee. As a new tube unit with its own Duratron housing or as a replacement tube in most housings.

WARRANTY

Dunlee's Material and Workmanship Warranty is our expression of confidence and your assurance of the highest production and inspection standards.

Learn more about the benefits of the new Duratrons by Dunlee Ask your X-ray dealer or write.

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A PICKER CORPORATION SUBSIDIARY
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BELLWOOD, ILLINOIS 60104



This "cow" stands out from the herd!

This is Pertgen-99m, the cow that doesn't leak. Nothing comes out until you're ready to milk it.

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Safety—underneath the Pertgen-99m Generator is the Rayshield™, Abbott's exclusive Radioisotope Shielded Dispensing Unit, that keeps radiation to operating personnel at a minimum.

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Economy—because Pertgen-99m is precalibrated, you get more useable activity at no increase in cost!

PERTGEN™-99m

TECHNETIUM Tc 99m GENERATOR KIT

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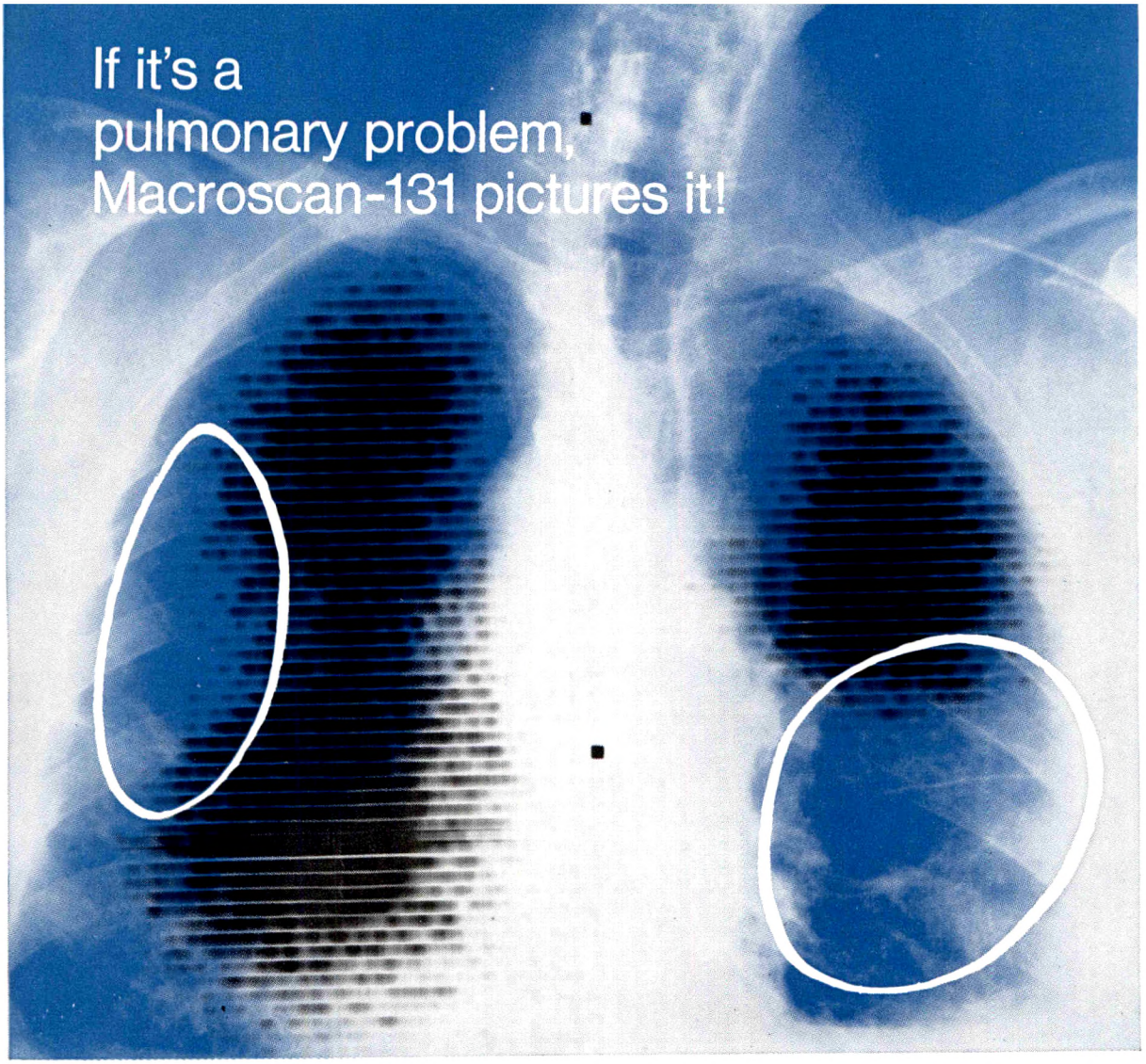
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World's Leading Supplier of Radio-Pharmaceuticals

LABOR-SERVICE GMBH, Abteilung RADIO-PHARMAZEUTIKA,
6236 Eschborn/Ts, Frankfurter Str. 20, Postfach 1245



A 70-year old man was admitted unconscious to the intensive care unit. Studies failed to reveal evidence of a myocardial infarction and the X-ray was not revealing. A pulmonary infarct was suspected and this diagnosis was established by a lung scan.

His posterior view scan above, showing diminished uptake in the left lingula and right lower lobe, was made with Macroscan-131. This product has many diagnostic uses:

Pulmonary embolism, suspected: To confirm (or rule out) its occurrence.

Chronic pulmonary tuberculosis: To estimate unilateral and regional function and perfusion of the lungs.

Emphysema: To evaluate the decreased regional blood flow that occurs with obstruction of vessels.

Pneumonitis: To evaluate the decreased regional blood flow that occurs without obstruction of vessels.

Lung Tumors: To evaluate the regional ischemia resulting from compression or obstruction of pulmonary arteries.

Surgery and/or other therapy for lung disorders: To evaluate the effectiveness of therapeutic measures.

Macroscan-131 is sterile and non-pyrogenic. It is ready to use and should not be heated prior to use.

INDICATIONS: For scintillation scanning of the lungs to evaluate total, unilateral, and regional arterial perfusion of the lungs.

CONTRAINDICATIONS: Radio-pharmaceutical agents should not be administered to pregnant women or to persons less than 18 years old unless the indications are very exceptional.

PRECAUTIONS, SIDE EFFECTS: Care should be taken to administer the minimum dose consistent with safety and validity of data. The possibility of an immunological response to albumin should be kept in mind when serial scans are performed. There is a theoretical hazard in acute cor pulmonale, because of the temporary small additional mechanical impediment to pulmonary blood flow. A possible case of urticaria has been related to a similar preparation. The thyroid gland should be protected by prophylactic administration of concentrated iodide solution. 903116

Macroscan™-131

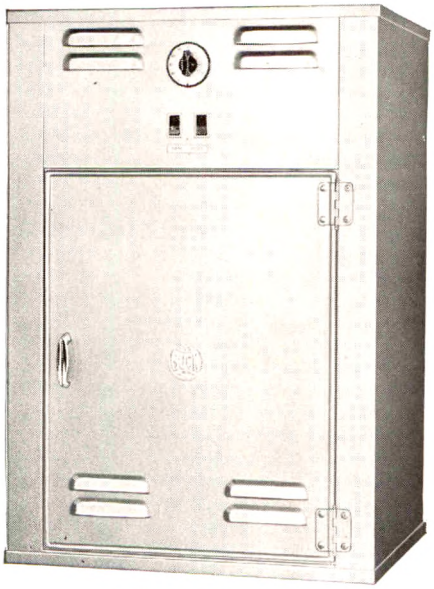
AGGREGATED RADIO-IODINATED (I^{131}) ALBUMIN (HUMAN)

ABBOTT LABORATORIES
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World's Leading Supplier of Radio-Pharmaceuticals
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BUCK X-RAY PRODUCTS

ITEMS NOW AVAILABLE FROM BUCK



CATALOG NO. 1050

MODEL 50 FAST DRYING FILM DRYER

Dries 12 X-ray films in 10 to 20 minutes. 60 minute timer controls the high capacity twin blowers which re-circulate air automatically pre-heated by two heating elements. Operating temperature pre-set at 125° F.

Pilot light; magnetic door latch; stainless steel hanger rack. Installation no problem — No exhaust ducts required. Operates on 110/125 volts 60 cy. AC. — 9.2 amps. Grounded 3 wire plug.

DIMENSIONS: Left to right, 23¼"; front to back, 18¼". Overall height 34".

FINISH: Baked-on mist-tan Std., mist-green, or gray-green.

STAINLESS STEEL MODEL MAGNESIUM FRONT CASSETTE

The world-famous BUCK Stainless Steel Hollow Frame Cassette is now available with a magnesium front faced with aqua, yellow, or white formica, black bakelite or baked on finish.

The new magnesium combination fronts are also available in the "All-Purpose" model Cassette. The magnesium front remains flat and is not subject to warpage from temperature changes.



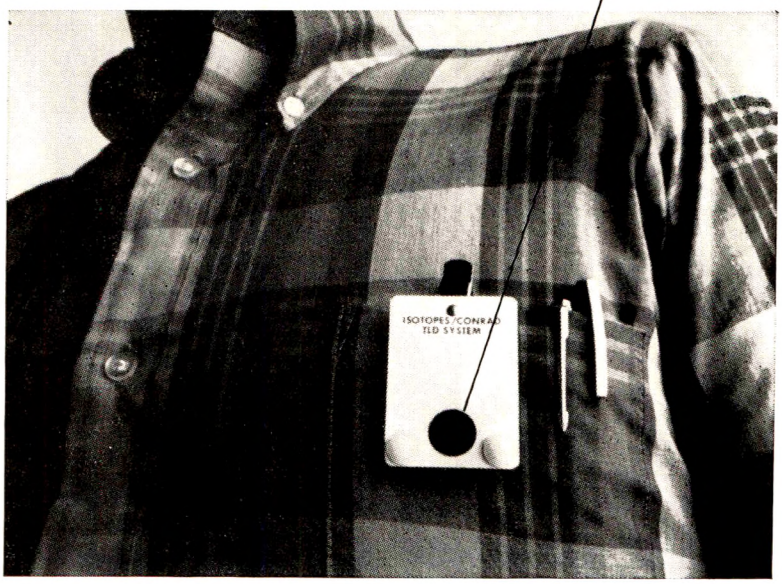
WHEN ORDERING BUCK CASSETTES - - - - ORDER THEM EQUIPPED WITH "BUCK SOIL-PROOF INTENSIFYING SCREENS."

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ISOTOPES NEW TLD BADGE SERVICE CAN TELL YOU A LOT MORE ABOUT YOURSELF.

Accurately, directly and fast. And in biologically significant terms. That's because the three tissue-equivalent LiF discs in an ISOTOPES TLD Badge are calibrated to tell you the precise dose to the skin, gonads and bone marrow. Then our TLD Readout Instrument prints out these dose records within a few minutes. No film processing, no checking calibration curves, no attempts at interpreting organ doses and no waiting as with film badges.

But there's even more. TLD Badges have a very broad dose range, 10 mrad to 10^5 rads. Particularly significant in accidents where immediate readout is vital. At the same time, the stability of TLD Badges over long periods of time recommends their use for low risk personnel, too.

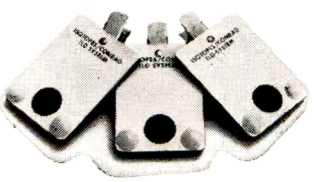
The Badge is extremely rugged, unaffected by temperature extremes, humidity, mechanical shock, light, water and most common solvents.

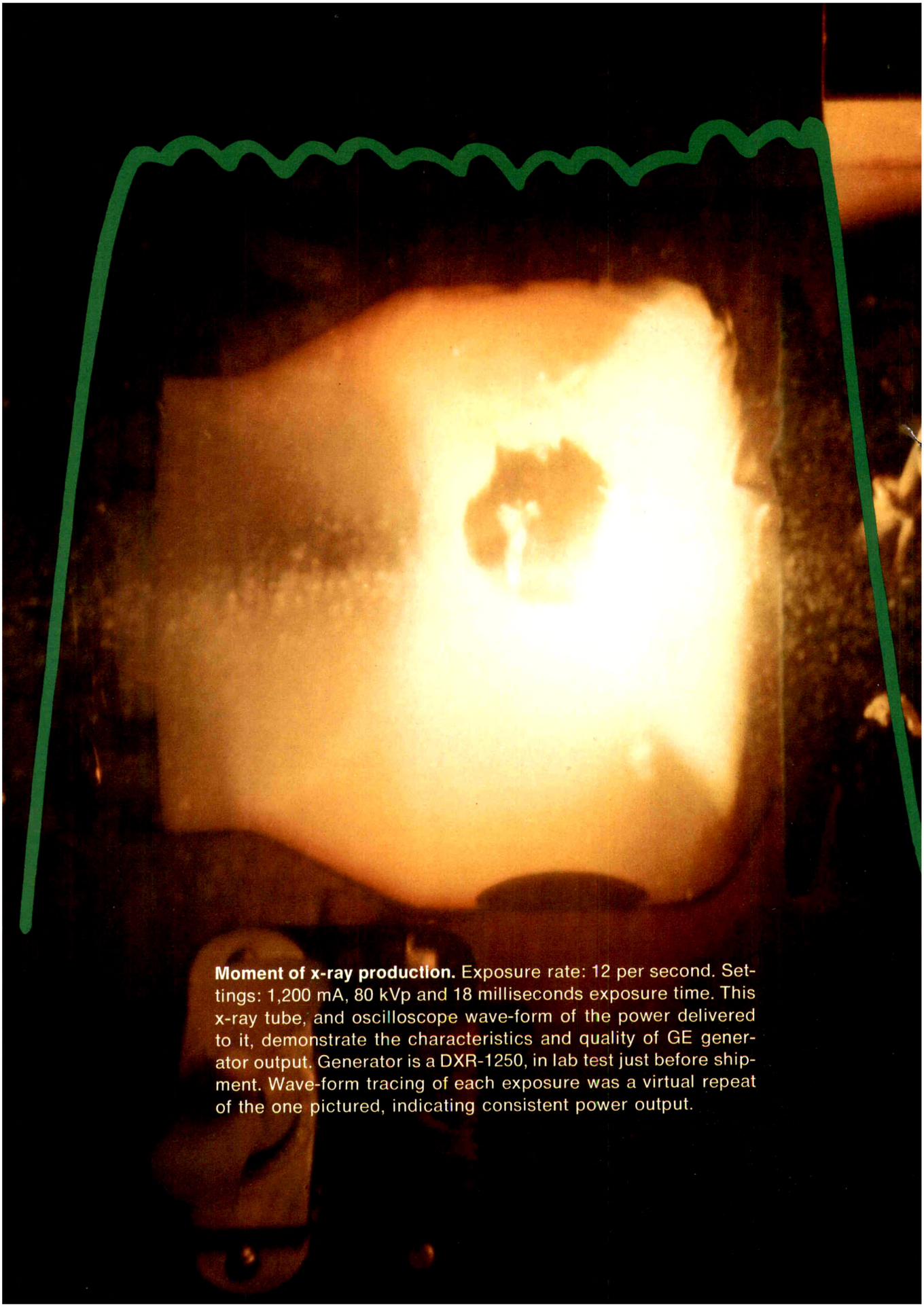
All in all, its ease of measurement and interpretation, long measuring periods and fast readout make savings possible for many categories of personnel whose doses are now monitored with film badges.

ISOTOPES TLD Badge Service is at your service. However, if you want to set up your own TLD Badge System with your own readout capability, we can help you do that, too. In either case, call or write ISOTOPES, 50 Van Buren Avenue, Westwood, N.J. 07675, (201) 664-7070.

ISOTOPES

A TELEDYNE COMPANY





Moment of x-ray production. Exposure rate: 12 per second. Settings: 1,200 mA, 80 kVp and 18 milliseconds exposure time. This x-ray tube, and oscilloscope wave-form of the power delivered to it, demonstrate the characteristics and quality of GE generator output. Generator is a DXR-1250, in lab test just before shipment. Wave-form tracing of each exposure was a virtual repeat of the one pictured, indicating consistent power output.

Precise Output at Tubehead Every Time—
Even for 12 Sharp Radiographs Per Second

Full power capacity to meet this test—every exposure, every patient—sets GE diagnostic x-ray generators apart. And ahead.

Face a problem like this and you'll agree: diagnosis of a congenital heart defect calls for a series of rapid exposures, at a rate of 12 per second. Exposure time must be short to stop involuntary motion. Useful kVp can't exceed 75-90, to retain good image contrast. Your only alternative, to get the desired radiographic quality: more current.

GE DXR-1250 3-phase, 12-pulse generator delivers it. Up to 1,200 mA at 90 kVp . . . plus exposure duration up to 18 milliseconds so you can still make 12 exposures per second, with average patients.

This is consistent power that meets full-rated capacity in fact, not just in theory.

Power that must be available—and usable—before all other elements in the x-ray system can work as they should. Power that reaches the tubehead with an absolute minimum of distortion and fall-off, so the kVp remains useful for producing quality radiographs.

Most important: because GE assures you the power needed for load extremes, you know you can count on precise power for your other x-ray technics.

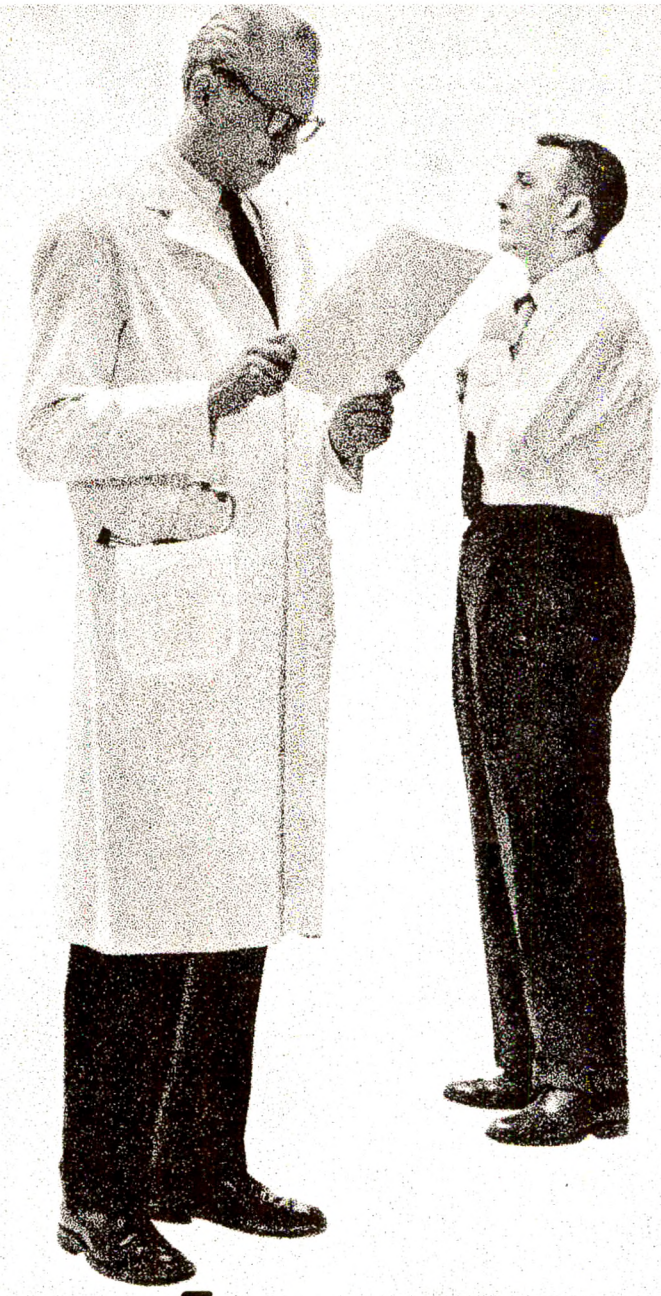
There's a GE x-ray generator with the power capacity and range that can help your diagnostic system reach its potential. Ask your GE representative for details. Or write General Electric, Electric Ave., Milwaukee.

The Generators with

GUTS

Enough to Assure All the Power You Need

GENERAL ELECTRIC



who goes for checkups?

A vital question. For if early diagnosis and treatment can cure cancer, obviously regular health checkups are essential.

In a survey conducted for the Society, we discovered that only 26% of those questioned had such regular checkups.

But 90% said, *if their physicians told them to do so,* they would have annual checkups. This confirmed what we have long known—your key role, doctor, in *activating* your patients in good health practices.

We alert the public with facts about cancer.

You follow through by urging regular checkups.

A life-saving combination.

AMERICAN CANCER SOCIETY

The human body virtually demands that its interaction with radiation be determined by indirect means.

Actual dose distributions cannot be measured in a patient, so the accuracies of the plan and its execution are unknowns.

When a treatment is planned for the Average-Man RANDO phantom or the Average-Woman RANDO phantom, actual dose distributions can be observed–by film, TLD dosimeters or miniature ion chambers.

RANDO test treatments reveal the accuracy of planning and disclose machine and human errors–wherever they occur. They can contribute a new order of certainty to the radiotherapy department.

Also available: The Phantom Patient for comprehensive basic training of Radiologic Technologists.



For new 12-page brochure, write to:

ALDERSON RESEARCH LABORATORIES INC.
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Density of a nucleus in any of the wide range of radioisotopes we make is of the order of 100 million tons/cm^3. That's compact. Like a mountain in a teaspoon.

But we shape it to our fussy pattern and get it to you on time every time. That's service.

From As^{74} to Xe^{133}, our range of radiopharmaceuticals is broad. And you can depend upon them for purity and stability.

All our radiopharmaceuticals with short half-life are advance calibrated. Emphasis on proper precalibration assures you of value as well as quality.

For top value, we also offer an exclusive Blanket Order Program.

All shipments are made the fastest way, usually the day we get your order. Because our home and 11 branch offices communicate by Telex. For fast order service, call our nearest office.

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our business is bringing Mountains to you, Dr. Mohammed



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AN ACTIVITY OF G. D. SEARLE & CO. AND THE RADIOCHEMICAL CENTRE



New seal of quality in world X-ray

You take the oldest name in diagnostic X-ray in the United States — Keleket: you match it to the first name in European X-ray — CGR. What's in it for you? The best of both worlds in a very special field — your own. It adds up to:

- the largest sum of knowledge in X-ray equipment — from 70 years of research, experience, and progress
- the most elaborate line of X-ray equipment ever marketed in the diagnostic field
- the kind of on-the-job reliability which doesn't come overnight, for which there is no substitute but year after year performance

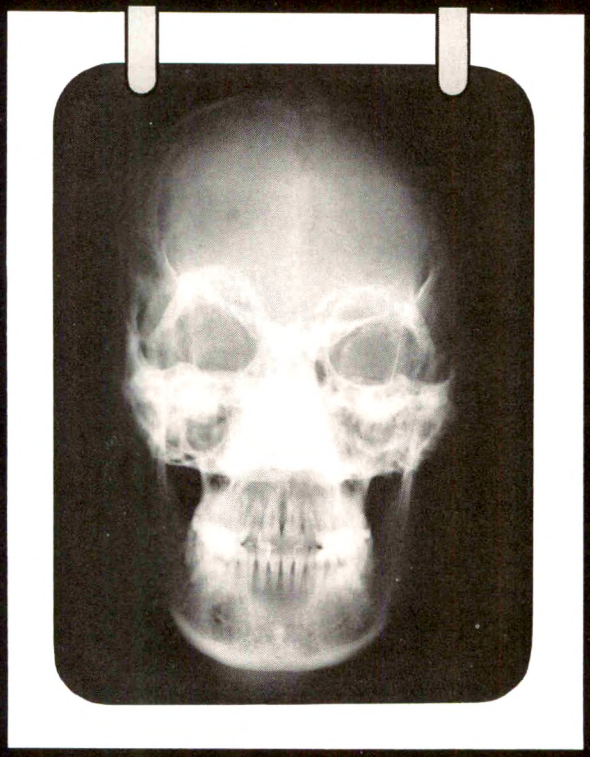
Look to Keleket/CGR for all these: • Conventional radiographic equipment • remote controlled radiographic equipment • cardiovascular equipment • neuroradiological equipment • tomographic equipment • mammographic equipment • image systems • constant potential generators • three-phase generators • solid state controls • mobiles • X-ray tubes.

A new brochure shows what 70 years of experience in the U.S. and Europe can mean to you. Write for it now.

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Medical X-ray Equipment • Accessories and Supplies

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- X-RAY TUBE
- FILTERS, CONES, AND APERTURE DIAPHRAGMS
- PATIENT
- DISTANCE
- GRIDS
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- X-RAY FILM
- PROCESSING
- FOG (ALL FORMS)
- VIEWING CONDITIONS



Any of these 11 factors can affect diagnostic clarity.

Du Pont has a new training seminar for resident radiologists that discusses each one.

This Du Pont seminar, entitled "Factors Affecting Diagnostic Clarity," is now being conducted in teaching hospitals across the country.

It demonstrates, with over 150 original radiographs, how the factors on the opposite page affect density, contrast, detail and distortion.

Residents tell us the seminar provides a better understanding of the radiographic process. It enables them to communicate more effectively with technologists.

We believe this seminar can be a meaningful supplement to the education of a radiologist. It results in better communication, fewer re-examinations and improved diagnostic clarity.

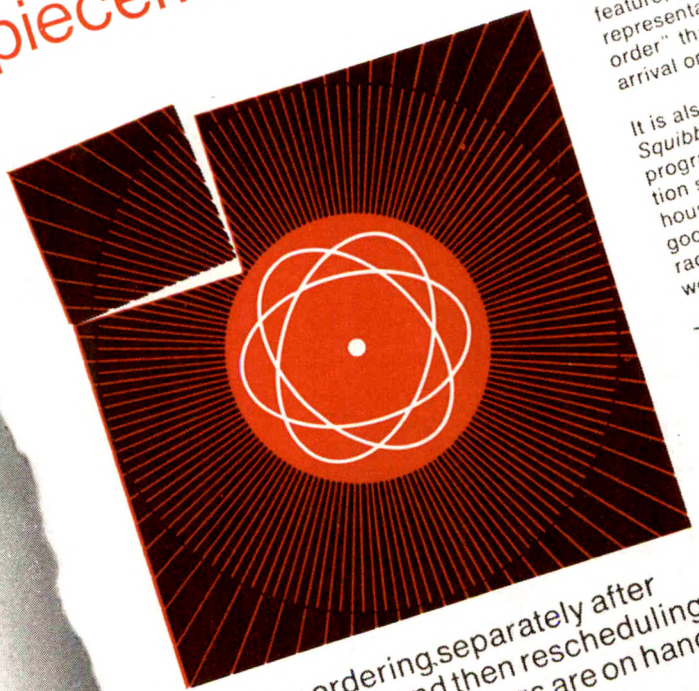
Training seminars are an important facet of Du Pont's focus on diagnostic clarity. Why not take advantage of them? Teaching institutions are invited to schedule this resident program through their Du Pont Technical Representative.

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SQUIBB

a research concept in radiopharmaceuticals

Are you ordering radioisotopes piecemeal?



Are you ordering separately after each referral and then rescheduling the patient? Most drugs are on hand when the patient needs them. Why not radiopharmaceuticals?

If a hospitalized patient needs blood, he can have it within minutes. If an ill patient needs penicillin, it can be prescribed immediately. But if he should need a radio-diagnostic test, he may have to wait several days for the material to arrive.

There was a time when such waiting was necessary, but no longer. Many of the available radio-pharmaceuticals have now reached the stage when they can be integrated into the mainstream of medical and hospital practice and can be "at hand" when needed. In particular, the unique 5-day precalibration of Squibb radioisotopes makes the need for ordering separately after each referral a thing of the past. Most laboratories can pretty well estimate what their approximate weekly need will be, so that everything can be ordered in one shipment to arrive on any given day. Thus, when a patient is referred, the diagnostic agent is already on hand and the test can be run immediately. Moreover, there is only one shipping charge. And if the material arrives for use during the latter part of the working week, Squibb will bear the cost of radioactive decay over weekends.

If you want to know more about this unique service feature, please contact your Squibb professional representative. He can arrange for a weekly "blanket order" that is shipped to you automatically for arrival on any day you specify.

It is also important that you know of the unique Squibb "*prefill*" *program* that anticipates and programs radiopharmaceutical parenteral production so that sterility and pyrogen test data are "in house" before the material is released. Thus, Squibb good manufacturing practices assure—even with radiopharmaceuticals—the same high standards you would expect in any regular parenteral preparation.

These are only a few of the many important features and services available to you when you use Squibb radioisotopes. Your Squibb representative will be happy to give you more details.

Medotopes®

Squibb Radiopharmace

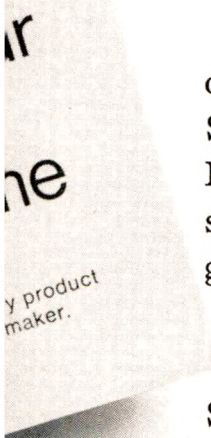
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precalibratio
lets you ha
entire wee
needs at

'The Priceless

SQUIBB is the honor a

This Squibb concept was bound to be emulated...

it's much easier to "follow the leader"



Unique service programs are hard to originate. But once established they *can* be emulated. And the unique Squibb 5-day Precalibration Plan was bound to be copied. For it has been eminently successful—offering significant savings in time, trouble and money to laboratories, as well as greater convenience and faster scanning service for patients.

Although others have now followed in our footsteps, reasonable facsimiles are not the original. For the broad Squibb experience and technical know-how that conceived and made the original plan possible has not been surpassed.

For details on the many important—and frequently unique—features and services available to you when you use Squibb radiopharmaceuticals, contact your Squibb Representative.

Medotopes®

Squibb Division of Nuclear Medicine
East Brunswick, New Jersey 08816

When we can't take a giant step, we take little ones.

B-D has been supplying the medical profession with surgical, diagnostic and therapeutic products of the highest quality since 1897.

The B-D name is a synonym for half a hundred practical advances in hospital and laboratory techniques. Like needles with specially-angled side bevels for consistent sharpness. Syringes with a positive lock that prevents accidental needle separation.

And disposability.

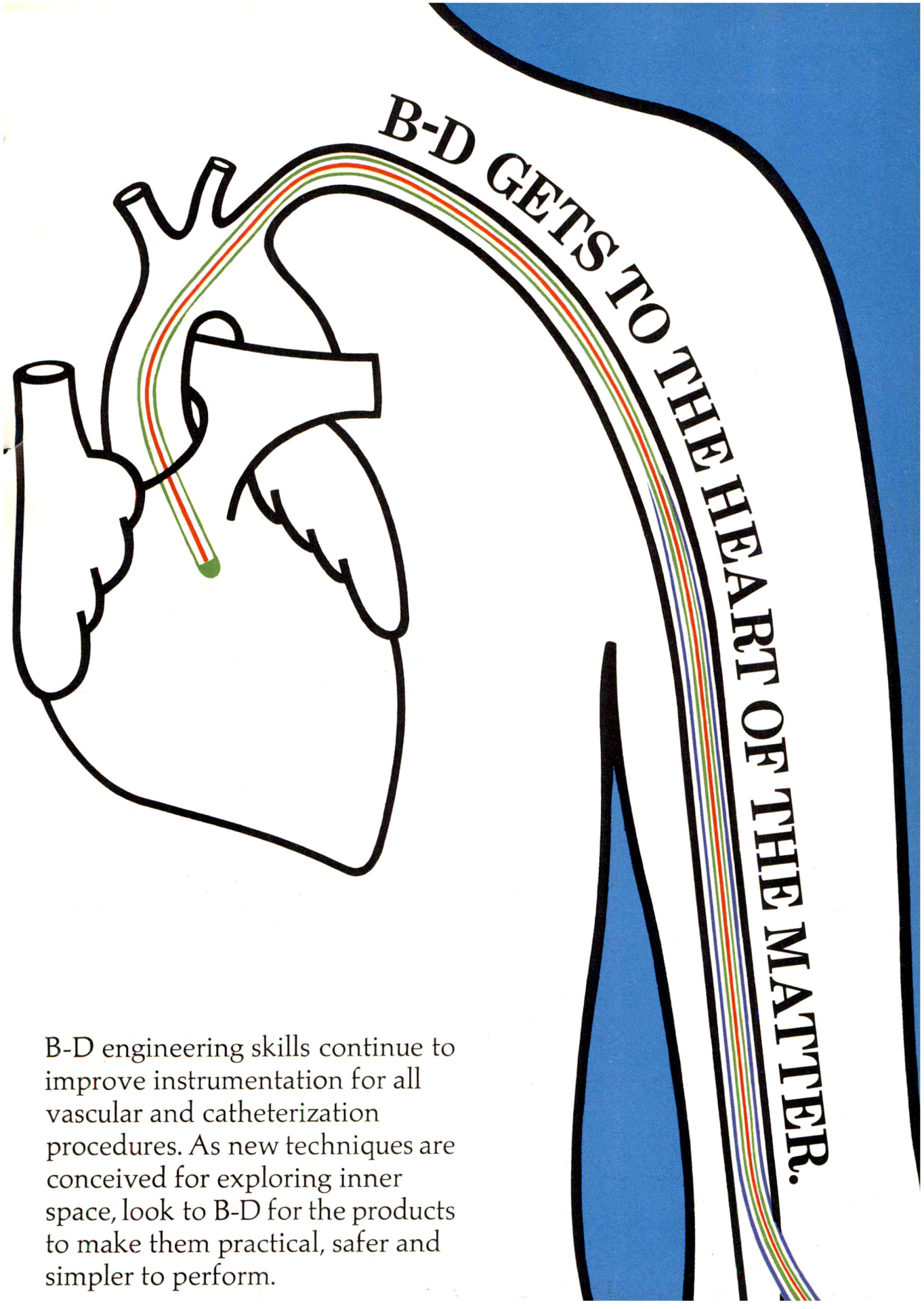
B-D also has long worked hand-in-hand with physicians and surgeons to develop variations in needles and instruments to meet their specific requirements.

When we can't take a giant step, we take little ones. Carefully controlled steps, with infinite attention to detail. Always in the same direction. Always aimed at freeing skilled hands from needless routine . . . at making it easier for you to use your skill to the fullest.

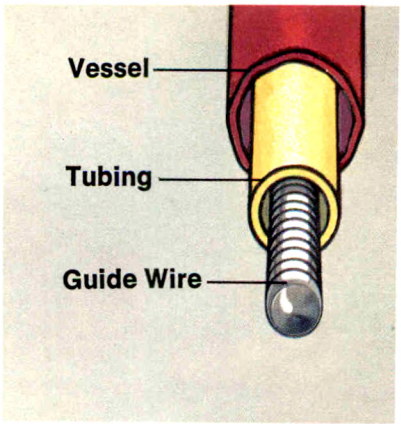
That's why everything changes at B-D but our name.

B-D

A step ahead in patient care.



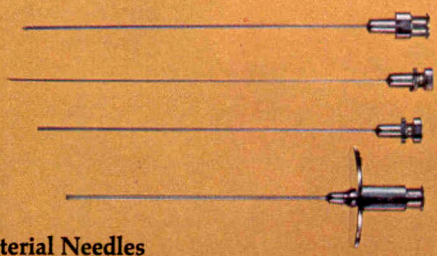
B-D engineering skills continue to improve instrumentation for all vascular and catheterization procedures. As new techniques are conceived for exploring inner space, look to B-D for the products to make them practical, safer and simpler to perform.



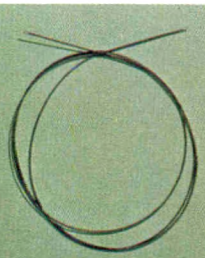
Precision products for arterial and venous catheterization.

B-D offers you a wide range of arterial and venous catheterization components for use in the Seldinger Technique of percutaneous catheterization . . . plus accessory items used in angiographic procedures. These products are precision made under the most exacting requirements to make sure that you have the safest instruments possible, capable of producing the most satisfactory results.

The Seldinger Technique eliminates the need for cutdown and arterial suturing, minimizes blood leakage as the catheter dilates the blood vessel. There's less trauma to the blood vessel; less discomfort for the patient. And the contrast medium may be injected at any desired level. In this procedure, the catheter is advanced over a flexible, stainless steel spring guide wire which had been previously introduced through a needle. Fixed or movable tapered inner cores facilitate easy passage within the blood vessel. (See illustration at left.)



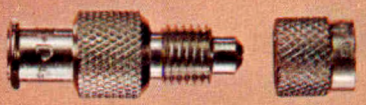
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Designed for accuracy and ease of handling. Consists of thin-wall outer cannula with blunt tapered point and LUER-LOK hub, an inner cannula with short bevel point and fitted stylet. Plus a blunt, rounded obturator for the outer cannula.



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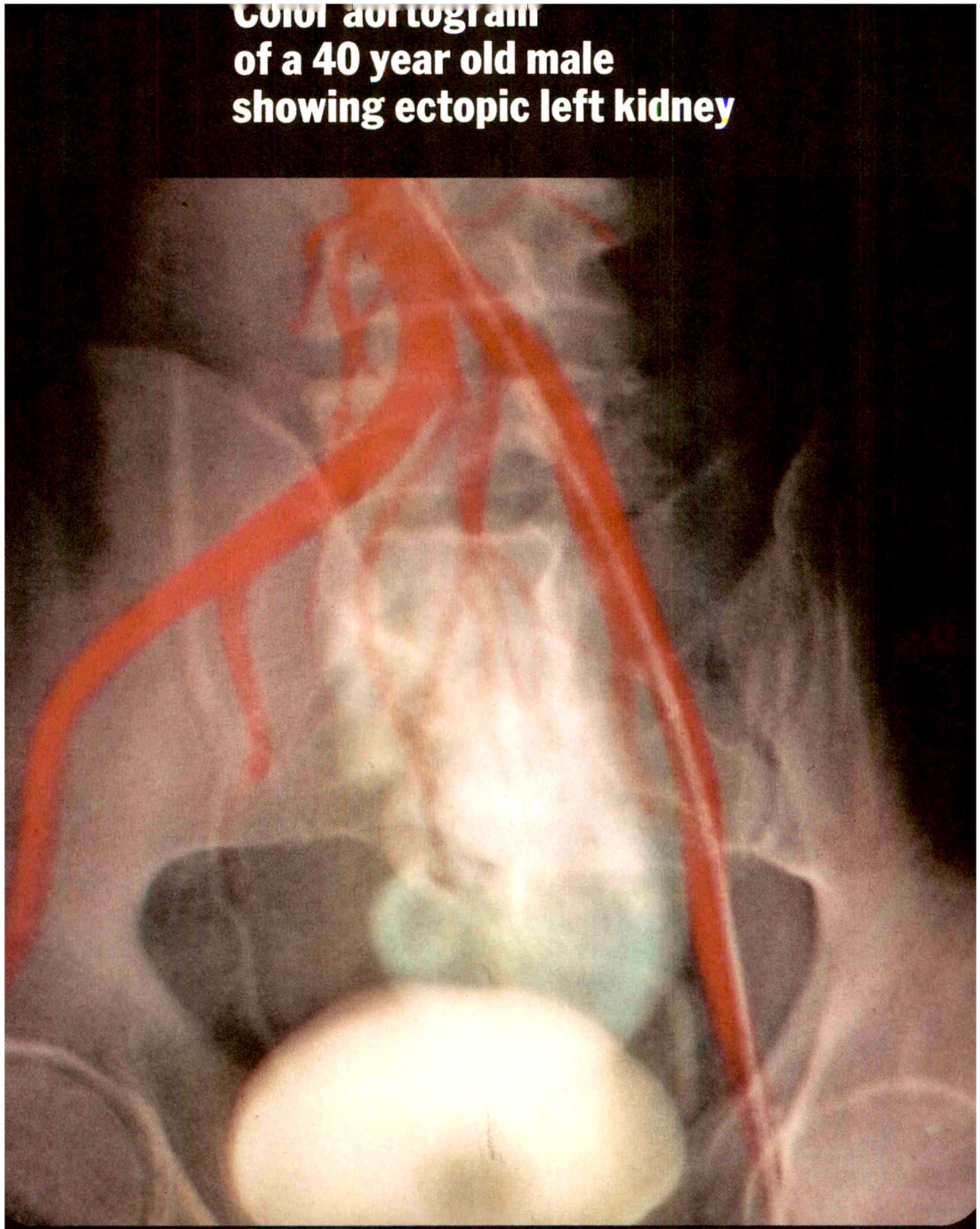


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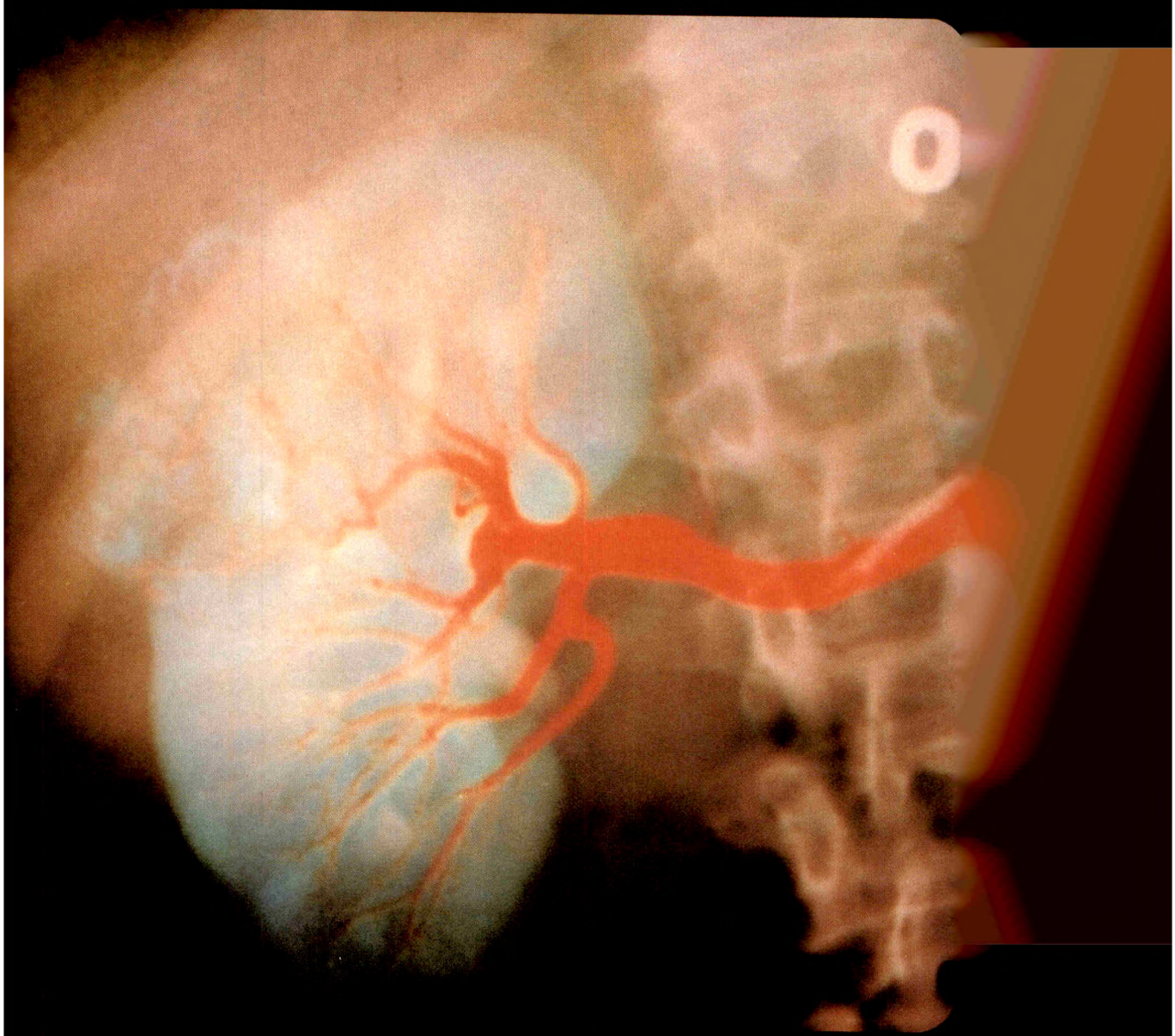
Color aortogram of a 40 year old male showing ectopic left kidney



he color films were prepared by a special technique by Robert L. Wise, M.D. of the Lahey Clini oundation and New England Baptist Hospital, Boston, Mass.

ypaque® sodium 50% (brand of sodium diatrizoate) is a versatile aid in the diagnosis of de variety of kidney conditions. Because of the fine detail obtained, **Hypaque® sodium 50%** lps delineate masses, cysts, vascular disorders, and anomalies or malformations of the kidney

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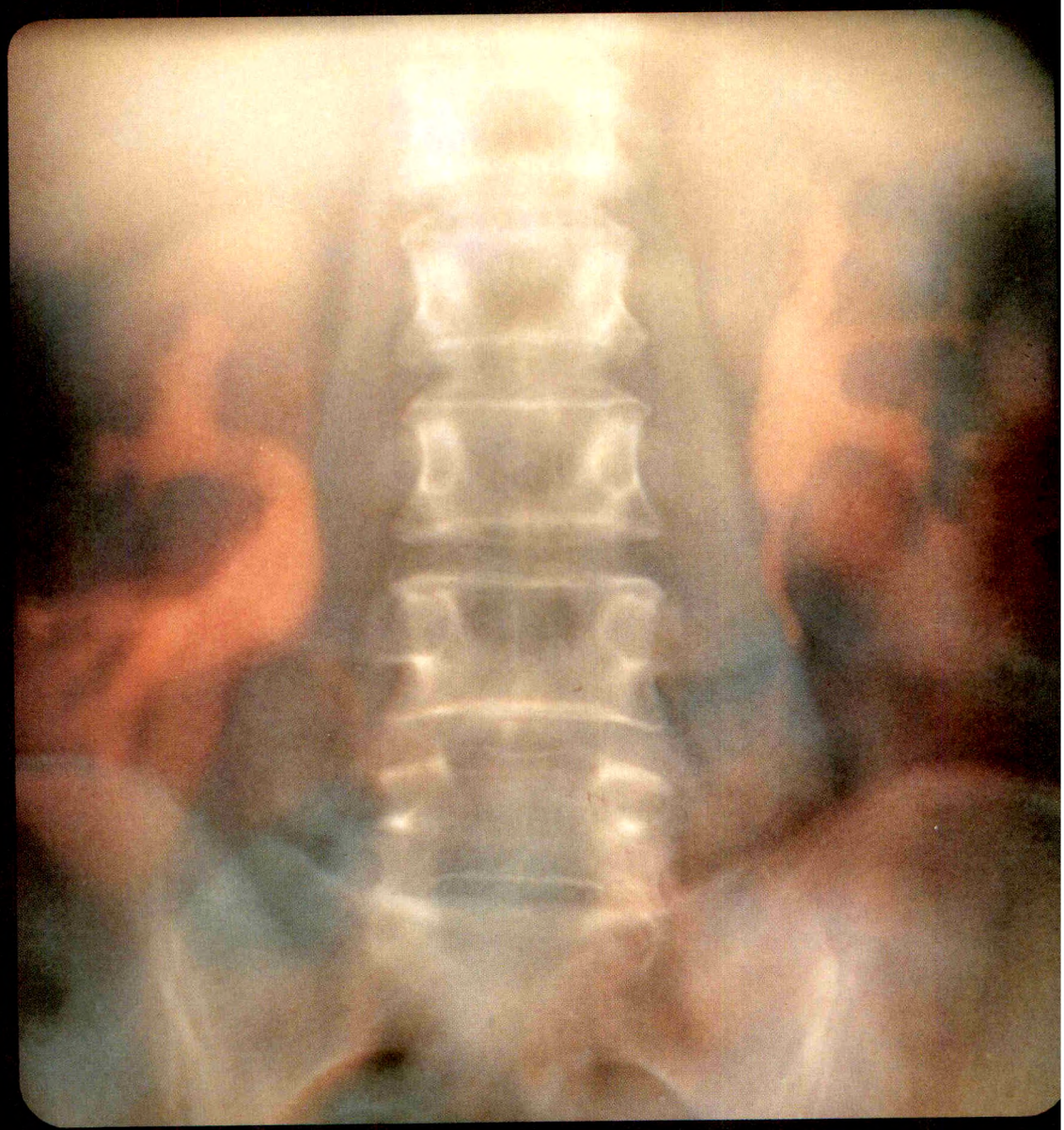


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Because **Hypaque® sodium 50%** has the *lowest viscosity* of *all* media for aortography and elective renal arteriography, the radiologist will find administration by needle or catheter easier aving time and effort.

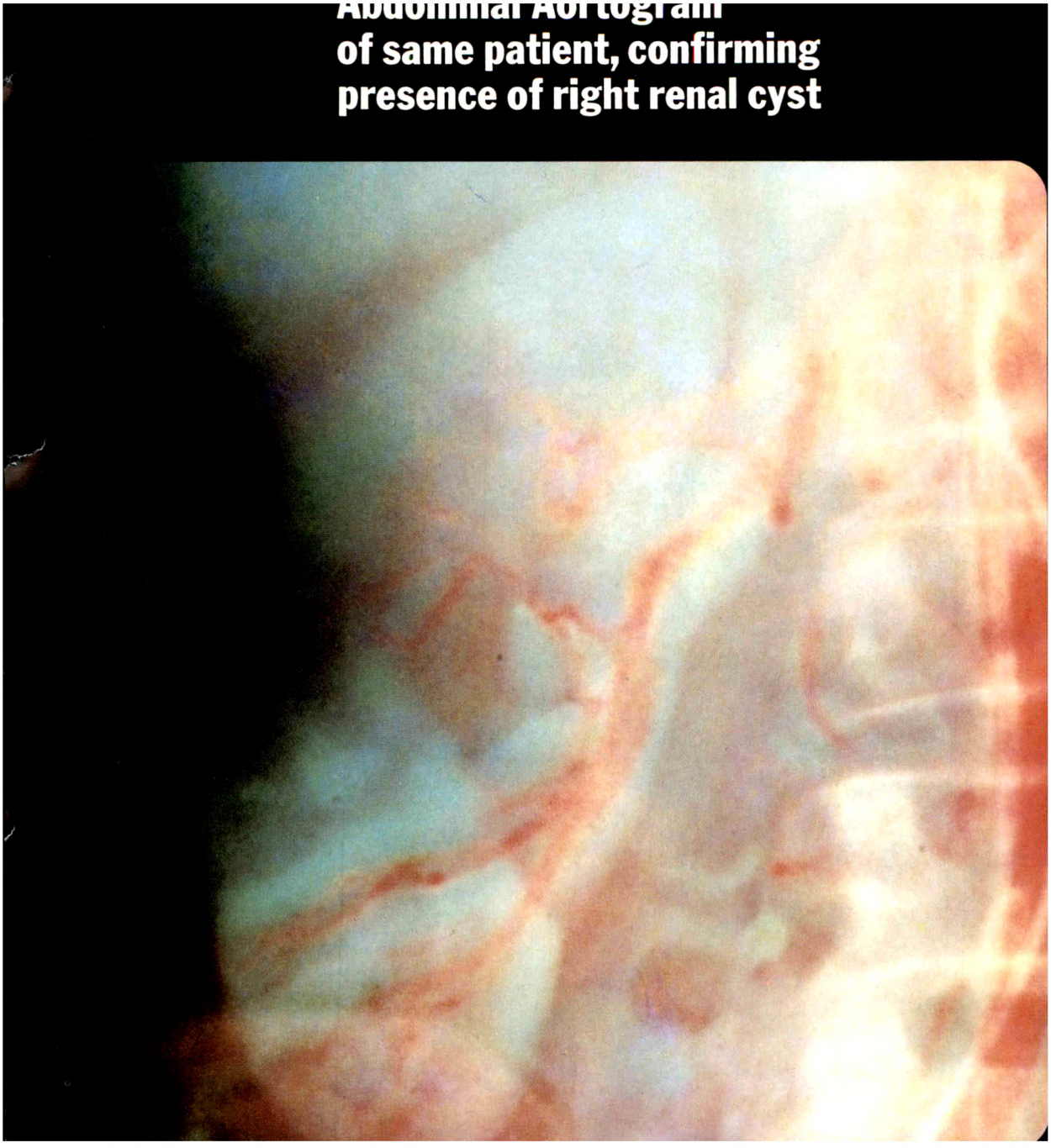
Please see last page for brief summary of prescribing in

of a 64 year old female suggesting large cyst, right kidney

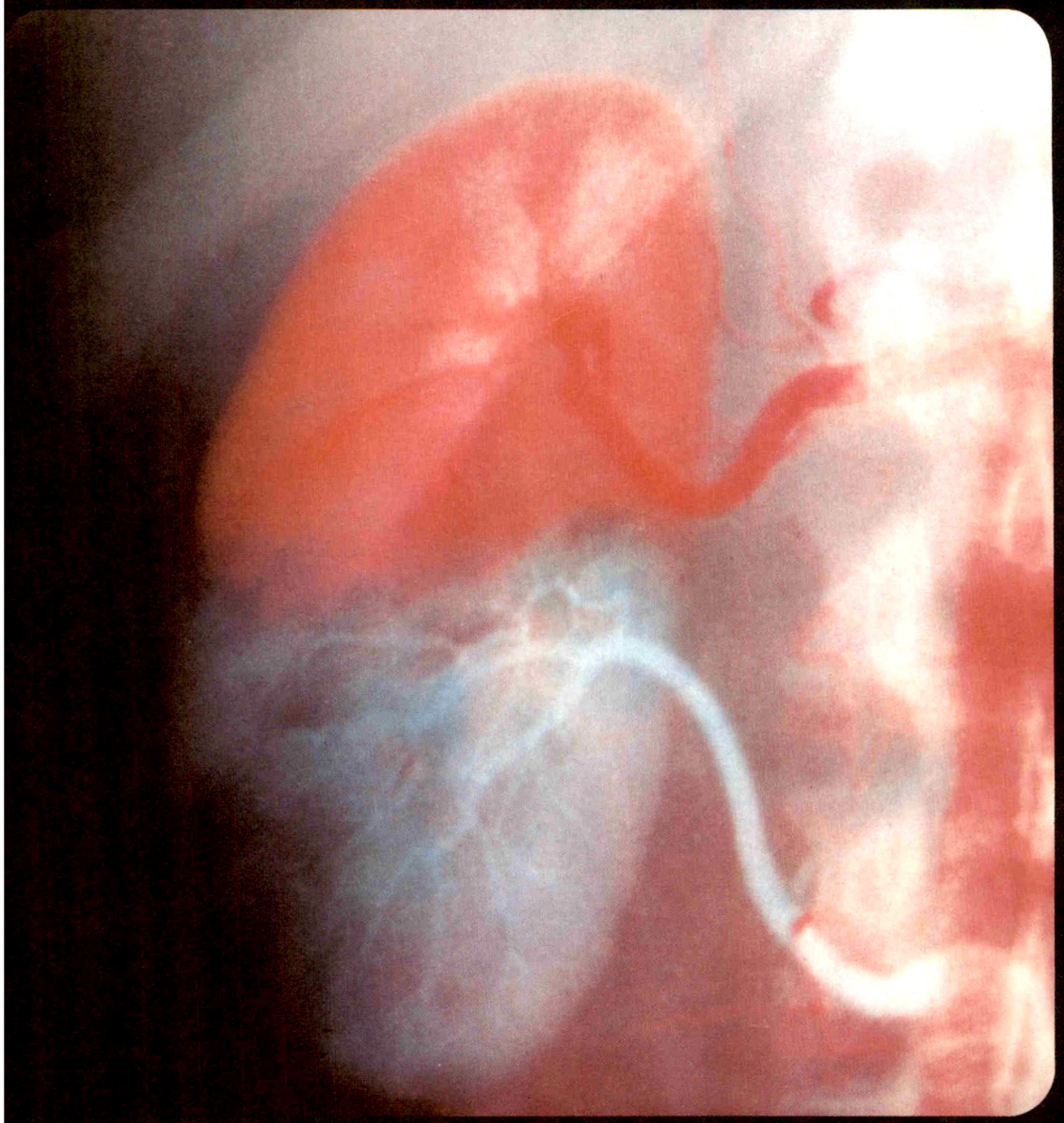


Using 300 ml. Hypaque® sodium in a 25% concentration, the radiologist can obtain valuabl
evidence in cases of renal abnormalities such as agenesis, duplication, ectopia, neoplasm or cys
When indicated, subsequent arteriography with **Hypaque® sodium 50% (brand of sodium di**
trizoate) will opacify the entire renovascular system for confirmation or for additional informatio

Abdominal Aortogram
of same patient, confirming
presence of right renal cyst



Color aortogram of a 38 year old male showing dual renal blood supply on the right



Hypaque® sodium 50% (brand of sodium diatrizoate) has optimal iodine content (300 mg/ml) and the advantage of low viscosity for accurate diagnosis and evaluation of major arteries in the kidney.

Angiography with **Hypaque® sodium 50%** helps supply valuable diagnostic information in demonstrating aneurysmal change or degree of patency of an arteriosclerotic vessel. It also aids the surgeon in determining if a stenotic vessel may be responsible for life-threatening hyper-
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Hypaque® 50%
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The versatile contrast agent for definitive renal visualization

Winthrop PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS

Please see last page for brief summary of prescribing information.

Summary of Full Prescribing Information

Hypaque® Sodium 50% brand of **sodium diatrizoate** Sterile Aqueous Injection (Weight/Volume)

Excretory Urography and Drip Infusion Pyelography

Description: Hypaque sodium is sodium 3,5-diacetamido-2,4,6-triidobenzoate, a radiopaque medium used to delineate internal structures.

Warning: Do not use Hypaque sodium for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

General and Specific Precautions: Caution is advised in patients with a history of bronchial asthma, other allergic manifestations, or of sensitivity to iodine; these conditions represent a special risk, though not an absolute contraindication. To avoid or minimize possible allergic reactions, premedication with antihistamines may be considered. Benadryl (diphenhydramine hydrochloride) in the same syringe with Hypaque may result in precipitation. A test dose of contrast medium is not entirely reliable. Severe reactions, including fatalities, have occurred with a test dose as well as with the full diagnostic dose.

Caution is advised in patients with severe cardiovascular disease. In patients with impaired renal function and cardiovascular disease, drip infusion pyelography imposes a sudden osmotic and sodium load which can precipitate congestive heart failure. Contrast media injected into arteries or veins can promote sickling of red cells in susceptible individuals. In patients with reduced renal function, repeat of excretory or retrograde pyelography should be delayed at least 48 hours to avoid temporary suppression of urine. In preparation for excretory urography of patients with multiple myeloma, partial dehydration is not recommended, since this may predispose to the precipitation of myeloma protein in the kidney tubules. When thyroid function studies (PBI and 24-hour radioiodine uptake levels) are indicated, they should be performed *prior* to radiographic studies or several days afterwards, to avoid inaccurate results.

Hypaque sodium 50% should always be injected at body temperature.

General and Specific Adverse Reactions: Adverse reactions, usually of a minor nature, have occurred in 10-14 per cent of patients who have received Hypaque intravenously. Reactions due to *faulty technique* include hematomas and ecchymoses, following extravasation from the vein, and pyrogenic reactions. *Hemodynamic reactions* include vasodilatation with flushing, hypotension and, rarely, vein cramp or thrombophlebitis. Serious *cardiovascular reactions* include rare cases of cardiac arrhythmias (e.g., ventricular fibrillation), shock, and cardiac arrest. Transient proteinuria may occur occasionally following the injection of radiopaques and, rarely, oliguria and anuria have been reported secondary to a hypotensive reaction. *Allergic reactions* include asthmatic attacks, nasal and conjunctival symptoms, cutaneous reactions such as urticaria and, rarely, anaphylactic shock, sometimes with fatal outcome. Severe reactions may also be manifested by signs and symptoms relating to the *respiratory system* (dyspnea, cyanosis, pulmonary or laryngeal edema), or to the *nervous system* (restlessness, confusion, or convulsions). *Other reactions* include nausea, vomiting, excessive salivation, anxiety, headache, and dizziness. Infrequently, "iodism" (salivary gland swelling) from organic compounds appears two days after exposure and subsides by the sixth day. Reactions to drip infusion pyelography may not appear until some hours after the examination.

Angiography (Peripheral Arteriography and Venography)

Precautions *(See also General Precautions):* Extreme caution is advised in considering peripheral arteriography in patients suspected of having thromboangiitis obliterans (Buerger's disease). Any procedure (even needling or insertion of a catheter) may induce a severe arterial and/or venous spasm. Caution is also advisable in patients with severe ischemia associated with ascending infection.

Adverse Reactions *(See also General Adverse Reactions):* In addition to those listed under General Adverse Reactions, are those due to arterial trauma during the procedure (i.e., needling, insertion of catheter, subintimal injection, perforation, etc.) as well as to the hypertonicity or effect of the medium; also reported are transient arterial spasm, extravasation, hemorrhage, hematoma with tamponade, injury to nerves proximal to artery, thrombosis (rare in venography, if vein is irrigated following injection), dissecting aneurysm, arteriovenous fistula, (e.g., with accidental perforation of femoral artery and vein during needling) transient leg pain from contraction of calf muscles in femoral arteriography; transient hypotension after intraarterial (brachial) injection, and brachial plexus injury with axillary artery injections.

Cerebral Angiography: Because of the special techniques required, it is recommended that Hypaque sodium be used for this purpose only by persons skilled and experienced in carrying out this procedure.

Contraindication: Carotid angiography should be avoided during the progressive period of a stroke, since this increases the risk of cerebral complications.

Precautions *(See also General Precautions):* Select patients for this procedure with care. Use the 50 per cent solution with caution in extreme senility (but not old age, *per se*), advanced arteriosclerosis, severe hypertension, and cardiac decompensation.

The diagnostic value of the procedure, according to many authorities, when employed early enough in locating lesions amenable to surgery, may outweigh the added risk to patients who have recently experienced cerebral embolism or thrombosis (stroke syndrome). A small number of postangiographic fatalities, including progressive thrombosis, have occurred in which the procedure did not appear to play a role. Patients with severe cerebrovascular disease may be examined primarily by indirect methods of angiography.

Care should be exercised to avoid contaminating catheters, syringes, needles, and contrast media with glove powder or cotton fibers.

Angiography is hazardous in subarachnoid hemorrhage. In migraine, the procedure can be hazardous because of ischemic complications, particularly if performed during or soon after an attack.

Adverse Reactions *(See also General Adverse Reactions):* The major sources of complications are faulty technique, occlusive atherosclerotic vascular disease, repeated injections of the contrast media, and higher doses than those recommended.

Untoward reactions are mostly mild and transient, although permanent visual field defects and deaths have been reported.

Vascular reactions: flushing, vessel spasm, thrombophlebitis, and cutaneous petechiae.

Neurologic complications: transient cerebral blindness, neuromuscular disorders, convulsions, coma, hemiparesis, unilateral dysesthesias, visual field defects, aphasia, and respiratory difficulties.

Aortography

Precautions *(See also General Precautions):* Special caution is advised to avoid inadvertent intrathecal injection when using the translumbar technique. The incidence and severity of reactions or complications that may occur are influenced by: the care and experience with which the procedure is performed; the amount and type of medium used; the age and condition of the patient; and the premedication and anesthesia used. Since aortography is not without some danger, it should be performed only by those experienced in the technique. Wherever possible, repeated injections of the solution during a single study should be avoided.

Adverse Reactions *(See also General Adverse Reactions):* Renal damage and shutdown; neurologic complications such as transverse myelitis or paraplegia; cardiovascular complications such as shock, cardiac arrest or failure, coronary occlusion, arterial thrombosis, embolism, and perforation of vessels; extravasation or hemorrhage from the puncture site or retroperitoneal catheter perforation; necrosis of the intestinal wall; acute pancreatitis; deaths; diffuse cutaneous petechiae; subintimal injection and aortic dissection.

Intraosseous Venography

See General Precautions and Adverse Reactions. A general anesthetic is sometimes necessary since the method is painful. Occasionally, extravasation of the contrast medium from the needle into the soft tissue may occur.

Direct Cholangiography

Precaution *(See also General Precautions):* This procedure should be used with caution in the presence of acute pancreatitis, injecting no more than 5 to 10 ml. without undue pressure.

Adverse Reactions *(See also General Adverse Reactions):* These may be attributed to injection pressure or excessive volume of the medium, resulting in overdistention. Such pressure may produce a sensation of epigastric fullness, followed by moderate pain in the back or right upper abdominal quadrant, which will subside when injection is stopped.

Some of the medium may enter the pancreatic duct and cause a transient serum amylase elevation 6 to 18 hours later, without apparent ill effects. Pancholangitis resulting in liver abscess has been reported. Occasionally, nausea, vomiting, fever, and tachycardia have been observed.

Hysterosalpingography

Contraindications: Menstruation, active or imminent; infection in any part of the genital tract, including the external genitalia; pregnancy, known or suspected. Use not advised for six months after end of pregnancy, or 30 days after conization or curettement.

Precaution *(See also General Precautions):* Caution should be exercised in patients with known or suspected carcinoma to avoid possible spread of the lesion by the procedure.

Splenoportography

Precautions *(See also General Precautions):* Procedure should be performed with caution on patients with blood dyscrasias, a tendency to severe bleeding, or a spleen recently become tender and palpable.

Adverse Reactions *(See also General Adverse Reactions):* Persistent hemorrhage with hemoperitoneum has been reported, and, in some instances, hemorrhage has required splenectomy.

How Supplied: Ampuls of 30 ml., boxes of 1, 10, and 25. A 1 ml. sensitivity test ampul is furnished with each ampul. Vials of 20 and 30 ml., rubber stoppered, boxes of 1, 10, and 25. Vials of 50 ml., rubber stoppered, boxes of 1 and 10. Each vial contains sufficient excess to permit withdrawal of 1 ml. for testing sensitivity.

If the solution is chilled, crystals may form but will readily dissolve if the ampul or vial is placed in moderately hot water before use. Cool to body temperature before injecting.

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EXPERIENCE WITH OVER 2,000 UTEROSALPINGOGRAPHIES*

By TOM M. FULLENLOVE, M.D.†
SAN FRANCISCO, CALIFORNIA

MOST radiologists, as most gynecologists, do not have the opportunity to perform a great number of uterosalpingographies and so do not have the opportunity to develop their technique to a point where they are proficient. With this point in mind, the author subspecialized in the procedure and personally did all the uterosalpingographies in patients referred to his group.

Lipiodol was not used from the beginning because of the many cases of granuloma formation that had been reported. We started the series using iodochlorol, which proved most satisfactory as it was a much more stable compound than lipiodol and would not break down to release iodine. When iodochlorol was withdrawn from the market, pantopaque was used for a short period of time and then ethiodol.

We have continuously employed opaque oily substances for 2 reasons: (1) we preferred the denser image produced; and (2) we preferred the 24 hour follow-up study, which the water soluble substances could not give us.

Over the years we have tried various aqueous solutions at one time or another, but were always disappointed because of lack of density, as compared with the opaque oils, and the fact that we were not able to obtain a 24 hour study. Another observation which was most striking to us —having used the opaque oils regularly— was the greater amount of pain experienced by women with the aqueous solutions.

At the present time we are satisfied with ethiodol and feel safe with its use.

TECHNIQUE

The sterile tray consists of the following: Jarcho cannula with collar; tenaculum; sponge forceps; 4×4 inch gauze flats; 1–3

* Delivered to the staffs of Keio University Medical School, Tokyo, Japan; Osaka City University Medical School, Osaka, Japan; Society of Obstetrics and Gynecology, Kyoto, Japan; Taipei Medical School, Taiwan; University of Hong Kong Medical School, Queen Mary's Hospital, Hong Kong; University of Basel Medical School, Bergerspital, Basel, Switzerland; and the Women's Clinic Hospital, Bern, Switzerland.

From the Departments of Radiology, St. Francis Memorial Hospital and University of California Medical School, San Francisco, California.

† Associate Clinical Professor of Radiology, University of California, School of Medicine; Radiologist, St. Francis Memorial Hospital, San Francisco, California.

inch No. 15 needle for aspirating the opaque oil from the ampule; 2–10 cc. Luer Lok syringes; gauze sponges; towels; medicine glass; large and small rubber acorns; and a speculum.

The patient is draped for pelvic examination on the fluoroscopic table and a small dose of an antispasmodic drug (octin, 1/2 cc. or another atropine-like drug) is given subcutaneously. A pelvic examination is done and the speculum inserted. Ten centiliters of opaque oil is drawn into the syringe and the cannula is filled to the tip end to eliminate air bubbles. The cervix is wiped clean of mucus and debris with merthiolate or zephirin. It is then grasped horizontally across the top with the tenaculum. The cannula, with either the large or small acorn positioned 1–2 cm. from the tip, is then placed in the os. Traction on the tenaculum and pressure on the cannula are maintained to prevent leakage. Both the tenaculum and cannula are tugged on together to flatten the genital tract and remove distortion. The speculum is then removed. These last two procedures are important, as the cervical canal and internal os may be obscured.

The patient is moved upward on the fluoroscopic table and each leg straightened. Under fluoroscopic control the opaque oil is injected, spot roentgenograms are made and the total amount of oil injected is recorded with each study. Using fluoroscopy there is no need for pressure recordings, as the filled uterus with resistance to injection is readily recognized. Venous intravasation is also immediately seen.

As long ago as 1932, Wong, Wu and Chien advocated that hysterosalpingography be performed under fluoroscopic control to prevent untoward reactions. They preferred to see how much filling occurred rather than rely on arbitrary pressure measurements (*Chinese Medical Journal*, Feb. 1932).

The procedure is explained to the patient and information regarding her menstrual cramps, if any, is obtained. It has been our experience that patients who have menstrual pain suffer very little from the examination, while those who have no pain suffer much more. We try to evaluate this and warn the patient.

Another point in developing this technique is the ability to be quick and sure so as not to overtraumatize the patient. Ordinarily she will have a small amount of spotting and she is warned about this and given a pad.

We have recently been using the vacuum-uterine-cannula (V.U.C.) of Malmstrom-Thoren and find it most satisfactory; however, there are certain lacerated or effaced cervices where the tenaculum must be used. This has occurred rarely in our practice, but the same tray set-up as previously described is still maintained as a standby.

The amount of cramping is much less with the V.U.C. and is associated with the placement of the cannula in the external os. Bleeding practically never occurs and the only spotting noted was related to a recurrence of the menstrual period.

We are using the V.U.C. in every patient now except in the rare cases of lacerated or effaced cervices.

CLINICAL APPLICATIONS

In the past 22 years in over 2,074 cases, we have tried to perfect a uniform technique in uterosalpingography so as to minimize the effect on the patient and to adequately demonstrate the cervix, internal os, uterine cavity, fallopian tubes and pelvic peritoneum. In doing so we have placed the greatest emphasis on the diagnostic criteria.

Practically all of our patients are examined for sterility or habitual abortion; nevertheless, in the course of our examinations, we have observed:

1. *Anomalies*. These vary from a completely double vagina, cervix and uterus (Fig. 1, *A* and *B*) to a slight dimpling of the dome of the uterus. Unicornuate uterus occurs in a good percentage of anomalies, but we must remember that histologically it is really part of a bicornu-

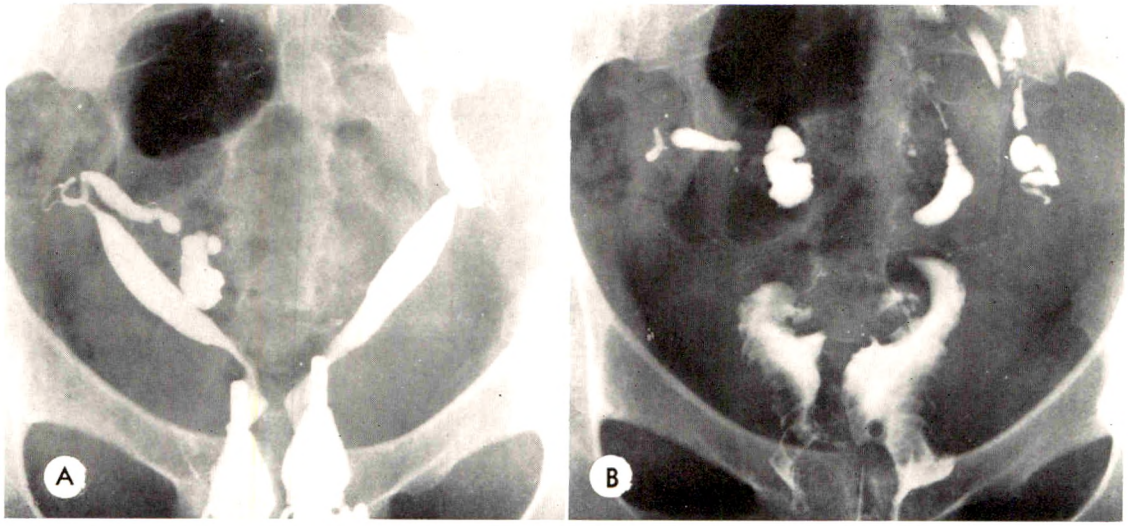


Fig. 1. (*A* and *B*) Double vaginae, cervices and uteri. Four years before, the patient had delivered a normal full term infant. Subsequent to this examination, she became pregnant and delivered a normal term infant. (*A*) Filled uteri, tubes and cervices. (*B*) Immediately after removal of the cannulae, double cervices and a vaginal septum are demonstrated.

ate development. Sometimes one side may be so rudimentary as to present no evidence externally; thus, we have a unicornuate uterus.

2. *Fibroids.* These may present as a smooth rounded intrauterine defect of the submucous type or as a marked stretching of the uterine cavity of the subserous type (Fig. 2). Removal of fibroids can leave a small or large defect in the uterine wall—a definite weak spot in case of subsequent pregnancy. Uterosalpingography should always be done following myomectomy, before allowing the woman to become pregnant.

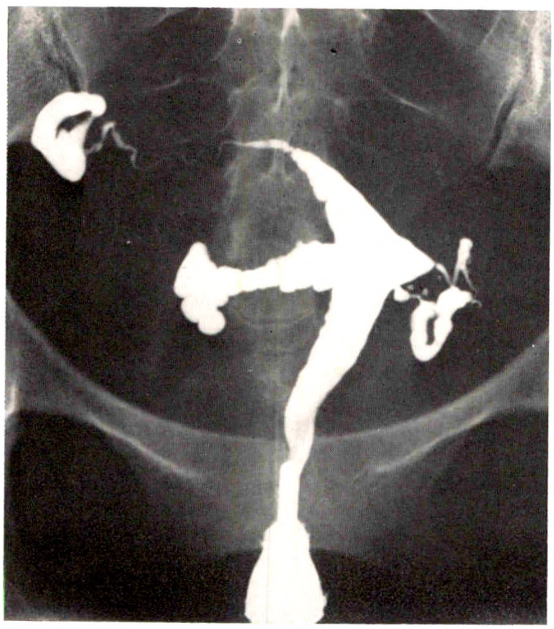


Fig. 2. Characteristic appearance of large uterine fibroid with stretching of the uterine wall and cavity.

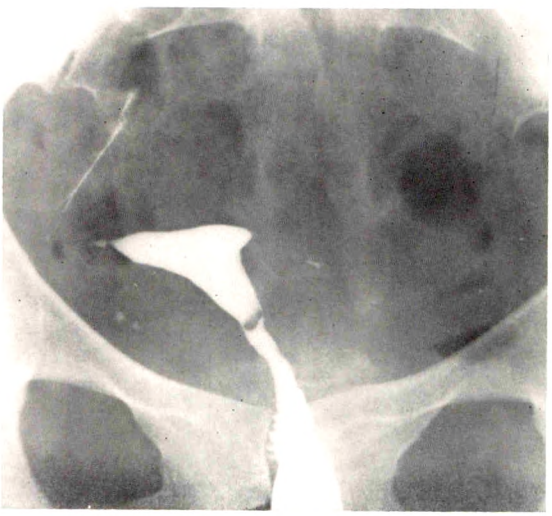


Fig. 3. Small polyp removed by dilatation and curettage. Under fluoroscopy it floated to and fro with injection or aspiration of the opaque oil.



FIG. 4. Defects caused by synechiae resulting from adhesions. These were removed at dilatation and curettage.

3. *Polyps*. If the polyps are sessile, they may be difficult to distinguish from submucous fibroids. If pedunculated, they can be seen to float and move back and forth under fluoroscopy (Fig. 3).

4. *Endometrial hyperplasia*. This is usually not a problem if the patient is examined within a week of cessation of menses. If present, it may simulate a number of conditions mentioned here.

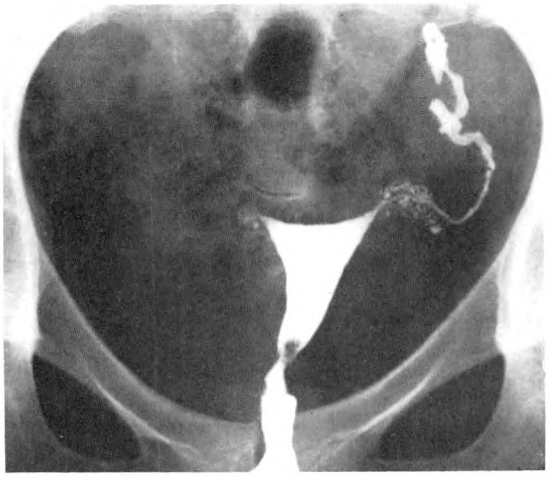


FIG. 6. Bilateral nodular salpingitis (salpingitis nodosa), so-called "diverticulosis" of the tubes. Small polyp also present at internal os.

5. *Adenomyosis*. This is represented by a few or many fine diverticulum-like projections from the cervical or uterine wall. It may simulate endometrial hyperplasia and may occur with fibromyomata.

6. *Intrauterine synechiae*. A bizarre scattered uterine pattern is presented which might simulate fibroids, adenomyosis or endometrial hyperplasia (Fig. 4). Curettage usually clears the adhesions, and sub-

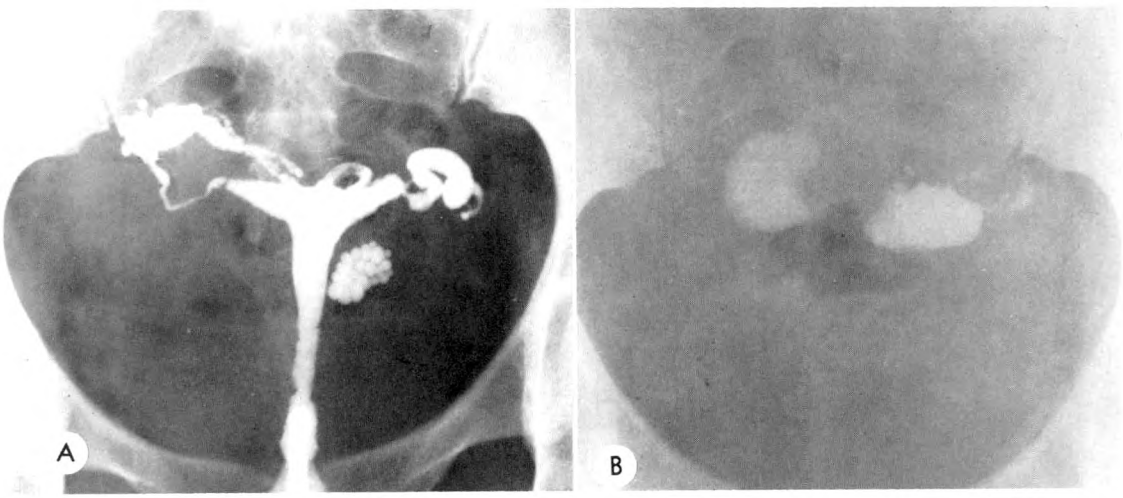


FIG. 5. (*A*) Bilateral tubal obstruction by hydrosalpinges and tubo-ovarian cavities not visible on the immediate study. (*B*) Twenty-four hour study demonstrates the tubo-ovarian cavities.

sequent uterography will show a normal contour.

7. *Tubal disease and defects.* Hydrosalpinx (Fig. 5*A*); tubo-ovarian cavities, which are usually very large pockets between the ovary and the fimbriated ends (Fig. 5*B*); kinking from adhesions; nodular salpingitis (salpingitis nodosa) (Fig. 6); or endometriosis; tubal occlusions from infection; tubal amputation and closure.

8. *Carcinoma of the uterus.* This usually presents in older women and shows a very irregular intrauterine pattern (Fig. 7). Venous intravasation occurs more often. The placement of radium may be facilitated by the visualization of the tumor. In the Orient we were shown cases of tuberculosis of the uterine body which resembled carcinoma (Fig. 8). We have never encountered such a case in our practice and, indeed, the clinical finding of tuberculosis of the uterine body is rare in the United States.

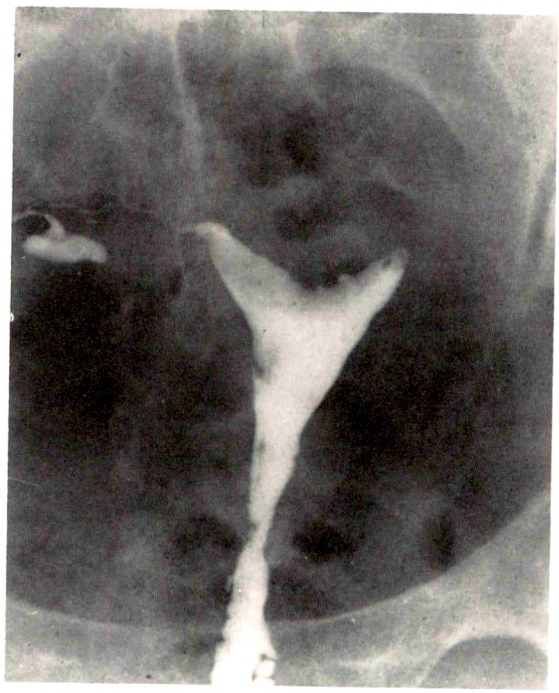


Fig. 7. Filling defects in the uterine cavity were carcinoma of the uterus. Except for the irregularity of the surface, the appearance is similar to that of a fibroid.

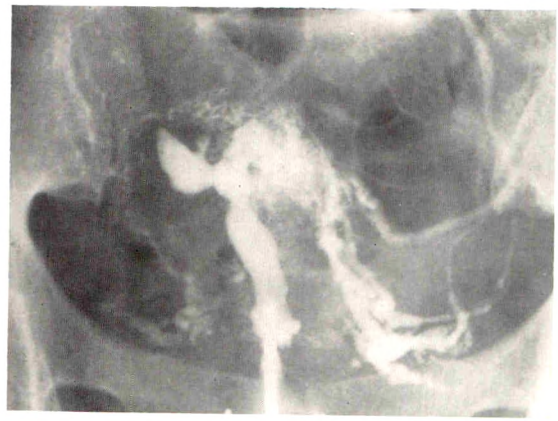


Fig. 8. Tuberculosis of the uterine body. Bilateral tubal occlusion. Venous intravasation occurred during the examination. Subsequently hysterectomy was performed. (Courtesy of Dr. Hisao Yamashita, Professor and Director, Department of Radiology, Keio University, Tokyo, Japan.)

9. *Cervical lesions.* Scarring from previous dilatation and curettage or instrumental abortion; hypertrophied plicae palmatae (Fig. 9), which can be so great as to cause cervical obstruction; actual stenosis; polyps; adenomyosis.

10. *Internal os.* Extreme spasm (Fig. 10, *A* and *B*; and 11, *A* and *B*); stenosis (Fig. 12); polyposis; dilatation or widening in habitual abortion (Fig. 13); scarring, as mentioned under cervical lesions.

11. *Ovarian tumors.* The 24 hour follow-

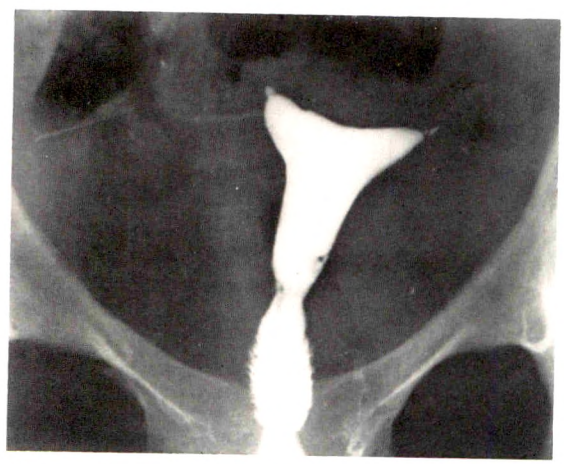


Fig. 9. Hypertrophied plicae palmatae. Some thickening of the endometrium in the lower uterine segment.

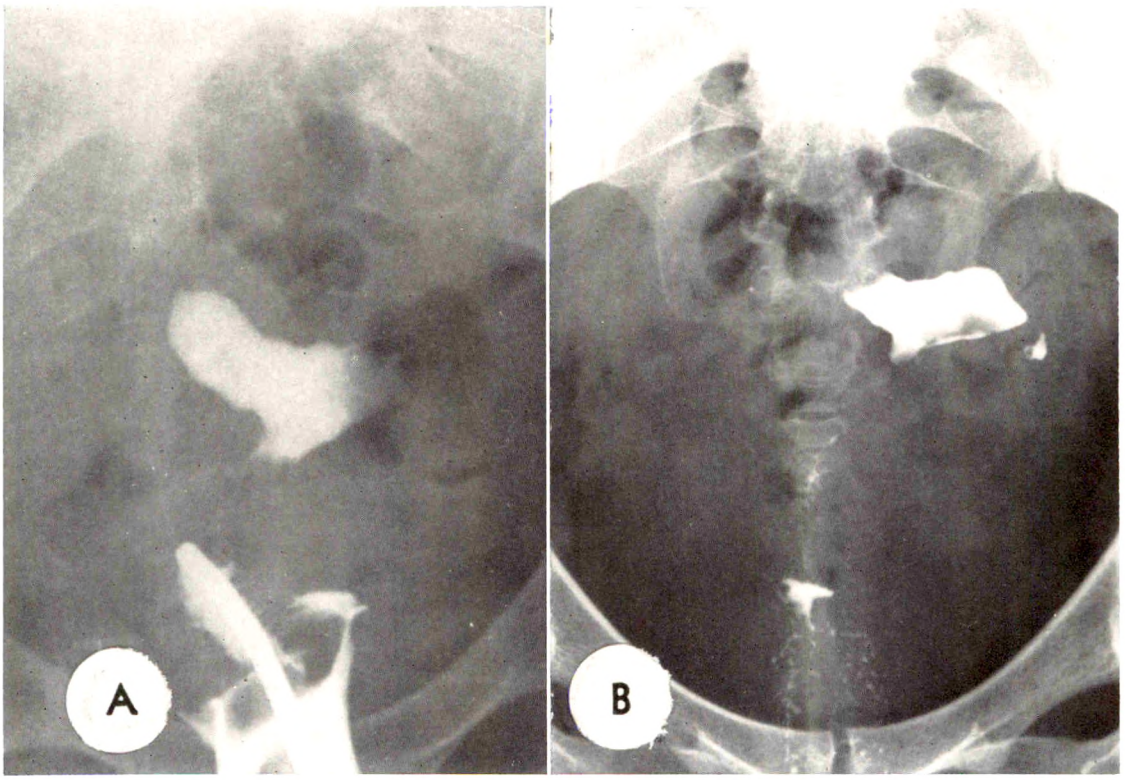


Fig. 10. (*A* and *B*) Extreme spasm of the internal os with considerable retention in the uterus in 24 hours. Patient very nervous and tense.

up study will often show the outline of pelvic masses, which combined with uterography can distinguish between fibroids and an ovarian mass.

12. *Pregnancy in infertile women.* Although no statistics were kept, it became evident through the years that infertile patients quite often became pregnant soon

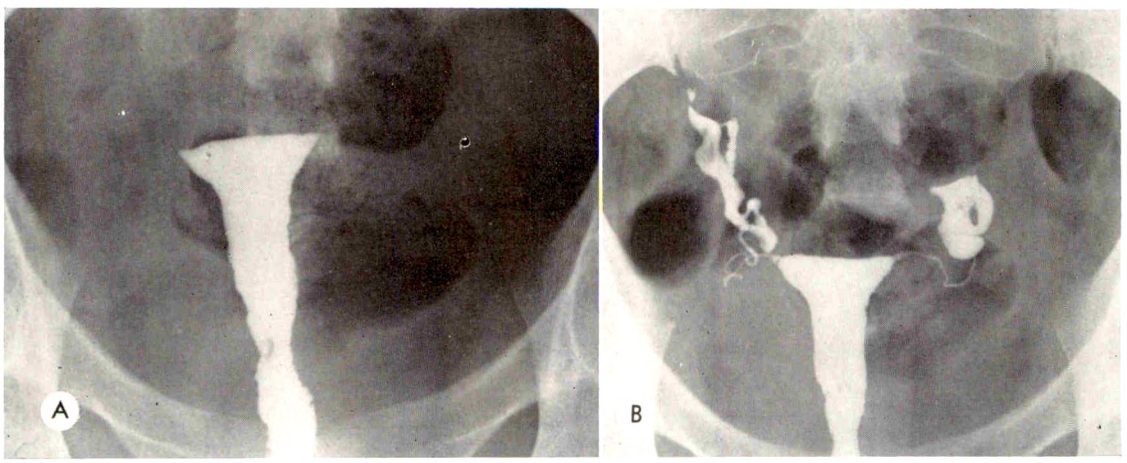


Fig. 11. (*A* and *B*) Patient very nervous and tense. (*A*) Study made without anesthesia; there is no filling of the tubes. (*B*) Study made under general anesthesia (pentothal); the tubes are outlined without difficulty.

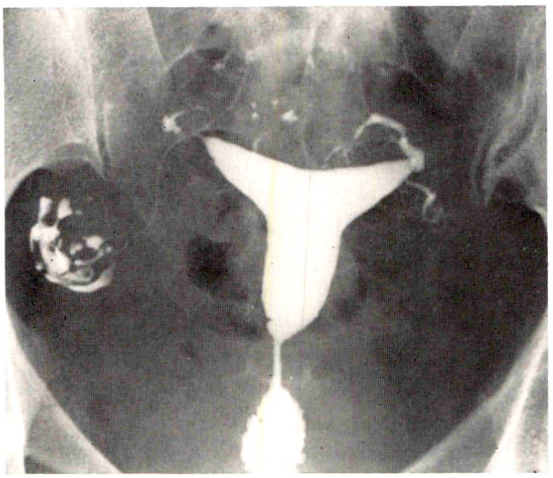


Fig. 12. Marked stenosis of the internal os from old inflammatory process.

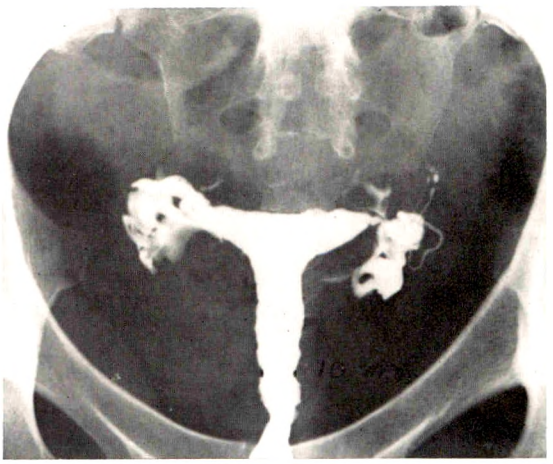


Fig. 13. Wide internal os, measuring 10 mm. (6 mm. considered upper limits of normal); parallelism of walls of internal os and cervical canal. The patient had had 10 miscarriages, all at 3 to 4 months gestation.

after uterosalpingography. Most of these patients had had several tubal insufflations and other treatment. We felt that this was due to the mechanical effect of the opaque oil in removing cellular debris or in opening the tubes by stretching fine adhesions.

COMPLICATIONS

Complications that can occur are: hemorrhage; flare-up of an infection; and venous or lymphatic intravasation.

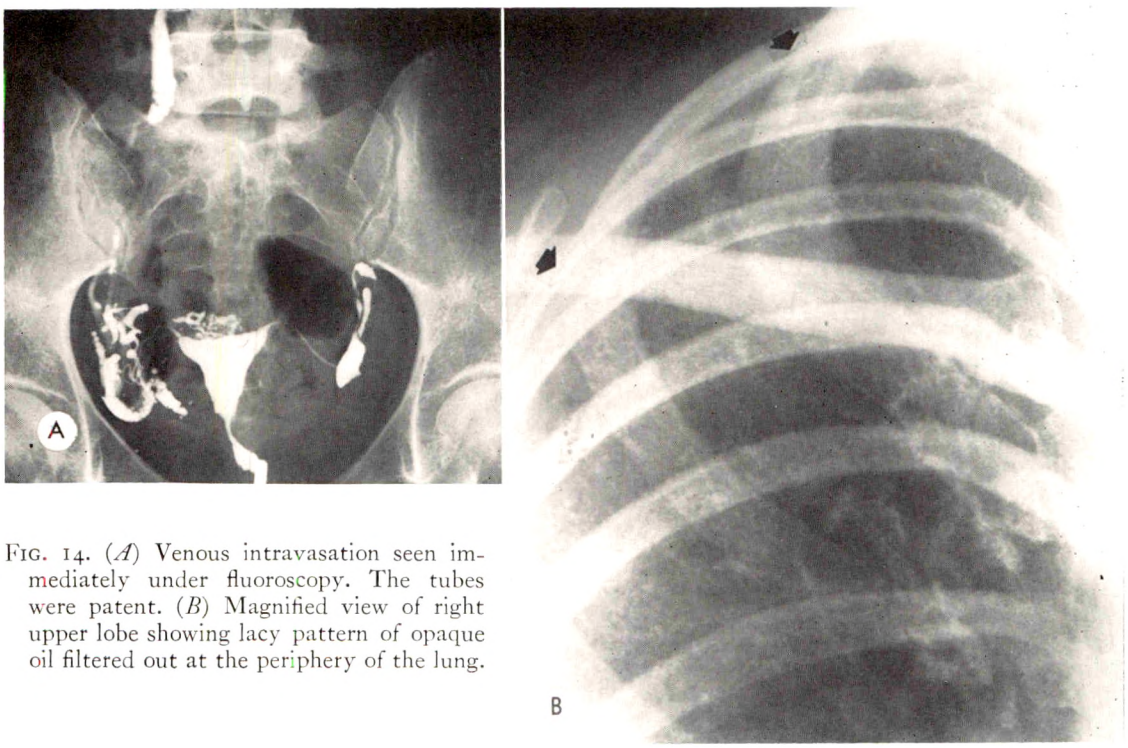


Fig. 14. (*A*) Venous intravasation seen immediately under fluoroscopy. The tubes were patent. (*B*) Magnified view of right upper lobe showing lacy pattern of opaque oil filtered out at the periphery of the lung.

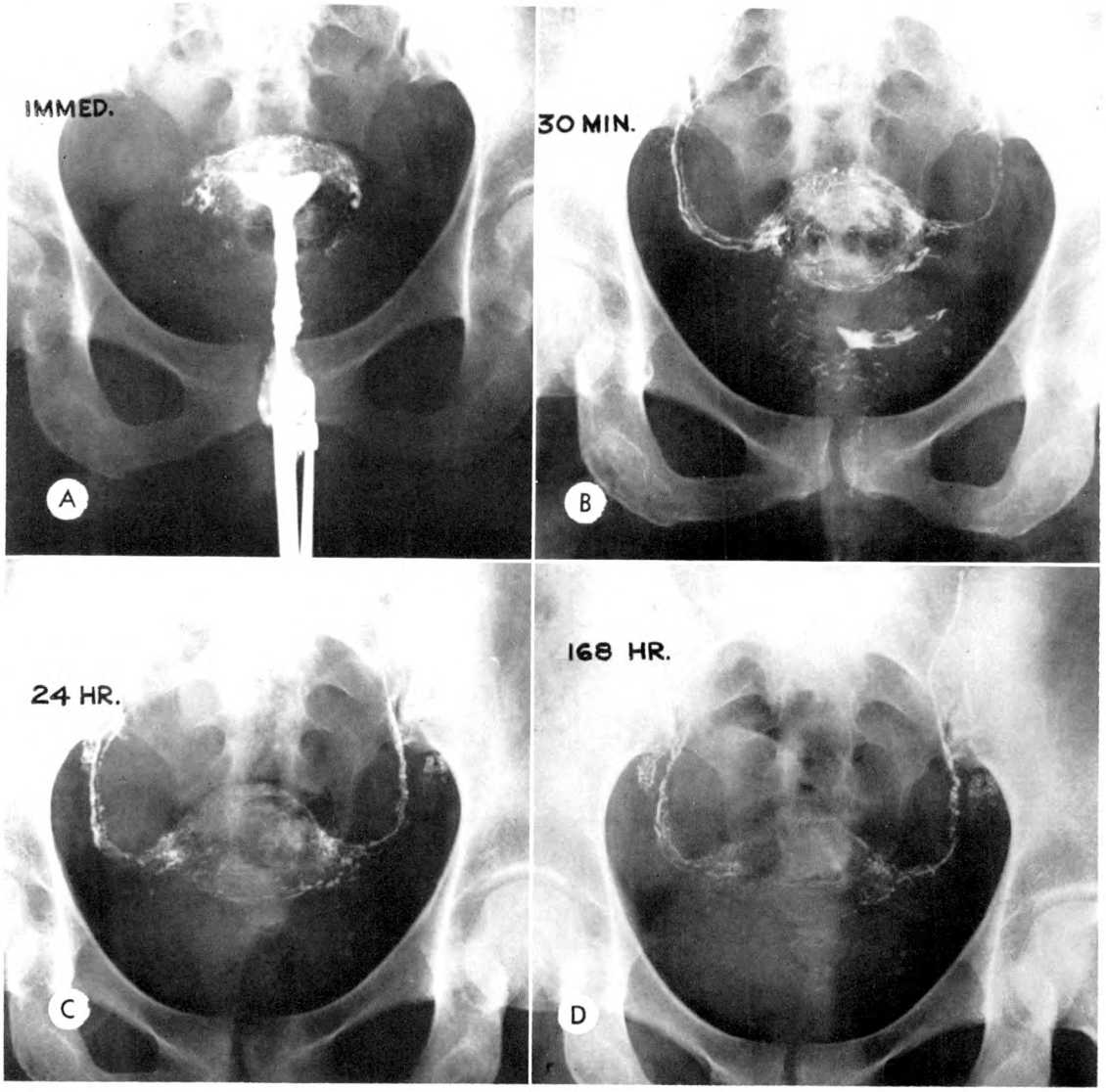


Fig. 15. (*A–D*) Lymphatic intravasation. Bilateral tubal occlusion. The patient was followed for 1 week. The lymph drainage of the uterus is shown.

1. Excessive bleeding is fairly rare and occurs when an artery or small arteriole is punctured by the tenaculum. Packing and/or coagulation usually control this complication.

2. If there has been a known pelvic inflammatory disease in the past, an antibiotic is administered prophylactically 2 to 3 days before the examination. If a flare-up occurs following the examination, antibiotics, bedrest, heat and sedation may be necessary. The examination should never be performed in the presence of an active infection.

3. Venous intravasation is readily recognized during fluoroscopy (Fig. 14*A*) and the examination is terminated at once. The opaque oil filters out in the lungs and can usually be seen if a chest roentgenogram is taken immediately (Fig. 14*B*). Follow-up studies show that the oil disappears in from 1 to 3 days, depending on the amount of contrast material injected. We have never had a reaction from intravasa-

tion, mainly because it was recognized immediately during fluoroscopy. This is one of the reasons why the examination should be done under fluoroscopic control. The reactions reported in the literature are primarily due to the injection of an excessive amount of the iodinated substance.

Lymphatic intravasation (Fig. 15, *A–D*) occurs with about the same frequency as venous intravasation. Both occur with increased pressure, denuded endometrium and, sometimes, without any discernible cause. Lymphatic intravasation causes no reaction and usually follows the same course of disappearance as in lymphangiography, namely 4 to 6 months.

Venous intravasation has occurred on 2 occasions when the puncture holes of the tenaculum inadvertently entered the cervical canal.

SUMMARY

A successful technique in uterosalpingography, used for over 22 years, is presented, together with the clinical applications and complications experienced by the author.

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NEUTRON RADIOGRAPHY IN BIOLOGIC MEDIA*

TECHNIQUES, OBSERVATIONS, AND IMPLICATIONS

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NEUTRON radiography has been used in industrial nondestructive testing for several years[8] but few investigators[1,8,9,25] have studied its potential for biologic applications. The contrasts in neutron radiographs of biologic specimens, however, are sufficiently different from those of conventional roentgenography that supplementary information can be obtained.

Neutron radiography, at present, can most easily be performed in the low energy region where both a sufficiently intense neutron source and an efficient neutron visualization system are available. However, fast neutrons will be necessary for sufficient penetration of most portions of the human body. Since suitable devices for visualizing fast neutrons efficiently have not yet been developed, the work reported in this paper is primarily concerned with low energy neutrons. Even though this research will probably have limited applicability to human diagnosis, it does lead to a clearer evaluation of the potential of this technique.

The purpose of this paper is to present the experimental procedures that were involved in taking neutron radiographs, give examples of low energy neutron radiographs of biologic specimens, and review the physical principles and special problems involved. The specimens that have been radiographed and are illustrated have been chosen to demonstrate the general properties of neutron images of tissue. The problems of high energy neutron radiography will be discussed in anticipation of the development of an efficient visualization system.

EXPERIMENTAL PROCEDURES

The technique of low energy neutron radiography of biologic specimens requires: (1) a high intensity source of low energy neutrons; (2) an antiscatter grid to be placed behind the specimen; and (3) a system to convert the image bearing neutron beam into a visual radiograph. Berger[8] has shown that the thermal nuclear reactor provides the highest neutron intensities. Atkins[1] and Parks and Brown[17] have demonstrated that the neutron scattering in the specimen (principally from hydrogen) has a decidedly deleterious effect on the quality of neutron radiographs, thus necessitating the antiscatter grid.

NEUTRON SOURCE

The Standard Pile (SP) reactor[2] at the Savannah River Laboratory was the neutron source for all the neutron radiographs of this report and is shown schematically in Figure 1. The graphite in the core slows down the highly energetic fission neutrons and scatters them into a 3 inch diameter flight tube in the graphite "thermal column." The beam thus produced has a diameter of about 4 inches at the position of the image recording foil.

The flux from the reactor was measured with standard foil techniques.[12,27] At the sample position, the thermal neutron flux (<0.5 ev. with average near 0.025 ev.) was about 3×10^6 n/(cm.^{2}) (sec.) when the reactor was operated at its maximum power of 8 kw. The total flux over that portion of the spectrum greater than 0.5 ev. and up to fission energies (2 mev. average) was approximately the same. The flux in

* Presented at the Sixty-ninth Annual Meeting of the American Roentgen Ray Society, New Orleans, Louisiana, October 1–4, 1968.
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the energy band from 0.5 to 2.0 ev. was about 4×10^5 n/(cm.^{2})(sec.).

In this paper, the term thermal neutron radiograph will imply that the radiograph was obtained primarily by the detection of the thermal portion of the neutron beam. The term epithermal neutron radiograph will imply the nearly exclusive detection of neutrons of energy greater than 0.5 ev. but usually less than 100 ev. The significance of the energy ranges given above will be demonstrated.

Antiscatter Grids.[17] Also shown in Figure 1 are the positions of the sample and the antiscatter grid. The thermal antiscatter grid had a grid ratio of 16:1 with 77 opaque lines per inch. It was assembled by stacking alternate $6\times1/8$ inch strips of 0.008 inch thick aluminum and 0.005 inch thick cadmium. An epoxy glue cemented the laminated sections. The epithermal grid was similar but had both thicker and higher strips, and used indium instead of cadmium to absorb the scattered neutrons (16:1 grid ratio with 27 opaque lines per inch).

Double cross-hatched grids were used initially, but eventually one grid was discarded since the slight gain in scattered neutron removal was obtained only with a considerable loss of line definition due to the increased penumbra that resulted from the necessarily larger specimen-detector separation.

A low frequency motor and cardioid cams imparted linear motion to the grid so that the line pattern was blurred.[17,18] These

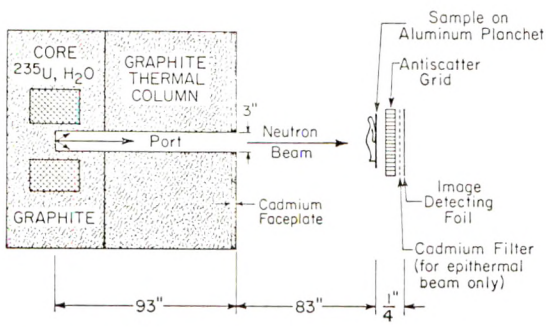


FIG. 1. The experimental arrangement for low energy neutron radiography using the Standard Pile Reactor (SP).

grid lines cannot be seen in the thermal neutron radiographs, but are discernible in the epithermal radiographs which were taken with an older design grid/oscillator.

Image Visualization. Low energy neutrons are poorly absorbed in normal photographic emulsions; thus, neutron imaging requires intensifying (converter) screens in a manner similar to conventional roentgenography.[9,25] However, unlike roentgenography, it is not always necessary to have the photographic film in contact with the converter screen during the irradiation. All of the neutron radiographs in this report were made by inducing radioactivity on a thin metallic foil that was placed behind the samples. Those neutrons that were unattenuated in the sample produced a radioactive "image" on the foil that subsequently yielded electrons by beta decay. The activated foils were recovered from the irradiation site, and the images on them were recorded on film by standard autoradiographic techniques. This transfer technique was used because the neutron beam was contaminated with γ rays, which would have caused interfering images. Berger has listed several of the more common transfer converter screens and their physical properties.[8]

The detector foil used in thermal transfers is usually made from material which has a high absorption cross-section and whose activated nuclei have a reasonably short half-life. Dysprosium was the transfer foil used for the thermal neutron radiographs of this report. It has a thermal activation cross-section at 0.025 ev. of 34.9 cm.$^{-1}$ and a half-life of 2.3 hours.

The detector foil materials for epithermal transfers usually have high activation resonance peaks in the epithermal cross-section. Indium, which was used for the reported epithermal radiographs, has a very large resonance from 0.5 to 2.0 ev., with the peak at about 1.4 ev. Moreover, the activated nuclei have a conveniently short half-life of about 54 minutes.

A sheet of 0.032 inch thick cadmium foil was placed in front of the indium foil

to prevent thermal neutrons from activating the indium. Cadmium has a very high absorption cross-section for thermal neutrons, yet its presence causes no undue loss of epithermal activations in the indium foil because of the low cadmium cross-section in the region of the 1.4 ev. indium resonance.

In the transfer technique, Kodak* Non-Screen Medical X-Ray (NS54T) film was placed in contact with the activated foil in a light-tight cassette for the estimated required film exposure using approximately one-fourth of the available emissions from the activated nuclei. The procedure was then repeated with new film for an adjusted period in case the first film was incorrectly exposed.

Specimen Preparation. Neutron radiographs of tumor specimens were taken prior to fixation. Control roentgenograms were made in the same plane using conventional mammography techniques. The tumor specimens were approximately 0.3×1.0 ×1.0 cm.

Arteriography specimens were prepared by injecting the contrast media (gadolinium oxide or indium oxide suspended in oil) directly into the aorta. Laboratory white rats weighing between 300 and 400 gm. were used. The injection was through a tapered polyethylene catheter (PE 205) inserted by open laparotomy. The animals were sacrificed immediately after the injection.

A ventriculography specimen was made by introducing air and gadolinium oxide into the ventricles of a dead rat by cisternal puncture. Direct ventricular and lumbar punctures were unsuccessful.

A tissue substitute test phantom was made from a lucite† wedge, 1 7/16 inches in its thickest portion. Two negative contrast agents, air and heavy water, and two positive contrast agents, indium oxide and gadolinium oxide were embedded in the lucite in parallel strips 1/16 inch high to form line pair phantoms of 32, 16, and 8 line pairs to the inch.

Dosimetry. The surface x-ray dose delivered to the various samples was measured with ionization chambers appropriate to the energy of the radiation used.[11] Comparable neutron doses were estimated from foil activation measurements[12,27] that were made by placing foils on the beam side of the tissue substitution test wedge. The thermal neutron surface dose was about 14 millirads per kilowatt-minute of SP reactor power. The epithermal surface dose in the vicinity of the indium resonance (0.5–2.0 ev.) was about 2 millirads per kilowatt-minute of SP reactor power. This does not include the surface dose from the epithermal neutron spectrum above 2 ev. To minimize the undetected dose from these higher energy neutrons, energy filtration such as can be obtained with crystal spectrometers[4] will be necessary. The gamma surface dose was found to be rather high in the SP reactor, about 71 millirads per kilowatt-minute.

The gamma to thermal and epithermal to thermal flux ratios in the reactor beam could have been greatly diminished by inserting bismuth and graphite sections into the end of the re-entry tube that is nearest the reactor core. Since surface dose was not of primary concern during these experiments, the beam from the core was left unaltered. The estimated surface dose of each exposure is listed in Table 1.

COMPARISON RADIOGRAPHS AND ROENTGENOGRAMS

Companion neutron radiographs and roentgenograms are shown for comparison for every specimen. The neutron radiographs were all made in the standard geometry of Figure 1. The roentgenographic prints in this report have had the very wide range of densities available in the original roentgenograms compressed by LogEtronic‡ techniques. This technique

* Kodak—Trademark of Eastman Kodak Co.
† Lucite—Trademark of du Pont Co.
‡ LogEtronic Incorporated, 7001 Loisdale Rd., Springfield, Va. 22150.

TABLE I

PHYSICAL FACTORS

Neutron Radiographs

Figure	Sample	Detected Energy	Adjusted Incident Dose* (rad)	Mean Free Path (mm. H_2O)	Detector	Grid	Neutron Exposure (kw.-min.)	Detected Thermal or Epithermal Surface Dose (rad)	Fraction of Available Decay Recorded on Film
2	Round steak	Thermal	0.6	3.0	Dy	⅛" Cd-Al	160	2.2	0.25
3	Rat chest	Thermal	5.6	3.0	Dy	⅛" Cd-Al	400	5.6	1.0
4	Tumor specimens	Thermal	0.2	3.0	Dy	⅛" Cd-Al	120	1.7	0.13
5	Rat paw and tail (Gd_2O_3 in arteries)	Thermal	1.4	3.0	Dy	⅛" Cd-Al	400	5.6	0.25
6	Rat head (In_2O_3 in arteries)	Epithermal	0.8	6.9	In	⅛" In Al	400	0.8	1.0
7	Rat head (air and Gd_2O_3 in ventricles)	Thermal	5.6	3.0	Dy	⅛" Cd-Al	400	5.6	1.0
8	Line definition test wedge	Thermal	1.7	3.0	Dy	⅛" Cd-Al	120	1.7	1.0
		Epithermal	0.7	6.9	In	⅛" In-Al	480	1.0	0.75

Roentgenograms

Figure	Sample	Estimated Incident Dose (rads)†	Approximate Mean Free Path of x rays (mm. H_2O)[14,24]	Equivalent Constant Potential kv.[14,24]	Technique	Control Settings			Filter	Focal Skin-Distance (inches)	Sample Backing	Half value Layer (mm. aluminum[11])		Exposure Rate[11] (r/min.)
						kvp.	ma.	sec.				hvl_1	hvl_2	
2	Round steak	720.	3.5	12	Grentz rays with panatomic x-film	15	5	1,200	None	15.5	None	0.06	0.06	40.
3	Rat chest	3.	15.	20	Conventional mammography	20	300	4	None	30.0	None	0.34	0.36	50.
4	Tumor specimens	3.7	20.	23	Conventional mammography	24	300	4	None	30.0	None	0.34	0.42	63.
5	Rat paw and tail (Gd_2O_3 in arteries)	0.2	44.	42	Conventional nonscreen	45	20	5	2 mm. Al	40.0	0.031 in. Al	1.2	1.7	2.4
6	Rat head (In_2O_3 in arteries)	0.2	44.	42	Conventional nonscreen	45	20	5	2 mm. Al	40.0	0.031 in. Al	1.2	1.7	2.4
7	Rat head (Gd_2O_3 in ventricles)	0.1	50.	55	Conventional nonscreen	60	20	0.008	2 mm. Al	40.0	0.031 in. Al	1.4	1.5	6.0
8	Line definition test wedge	0.2	44.	42	Conventional nonscreen	45	20	5	2 mm. Al	40.0	None	1.2	1.7	2.4

* Dose required if the autoradiographic exposure times had been optimized. Calculated by multiplying the measured thermal or epithermal entrance dose by the fraction of available decay actually used; dose from backscatter included.

† Assumptions: Water density tissue; ICRU (1956) roentgen to rad conversion factors at kvp. meter readings[21]; dose from backscatter not included.

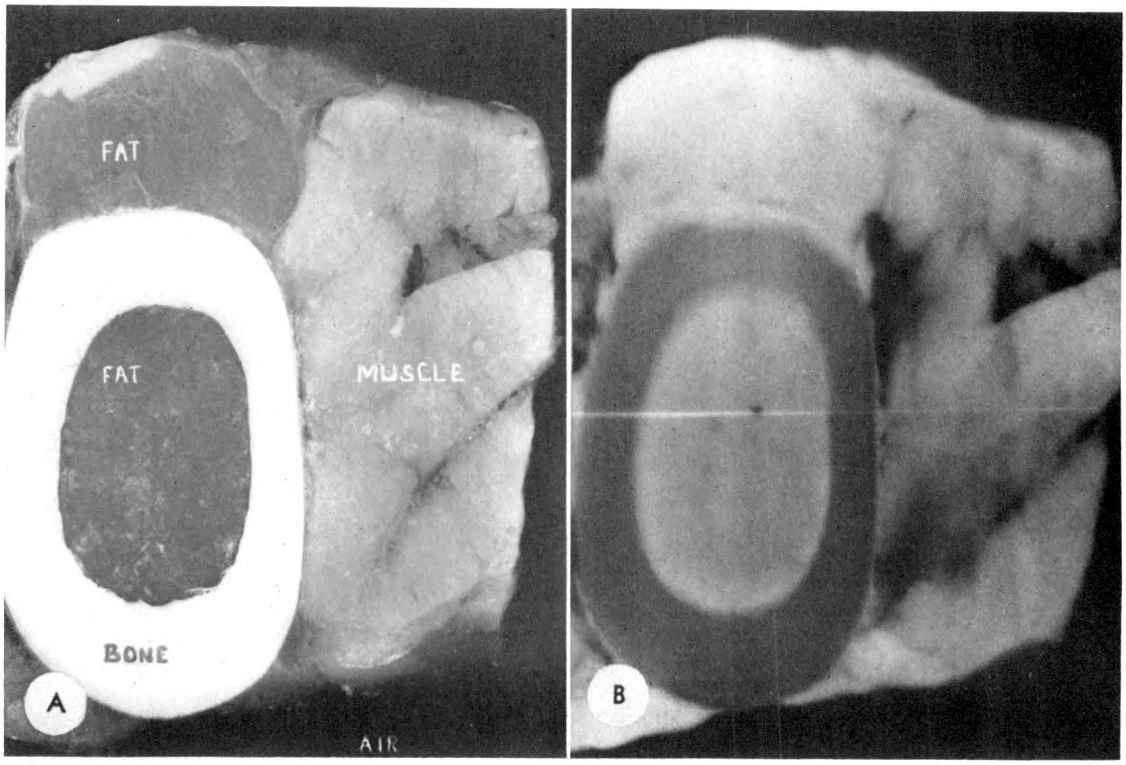
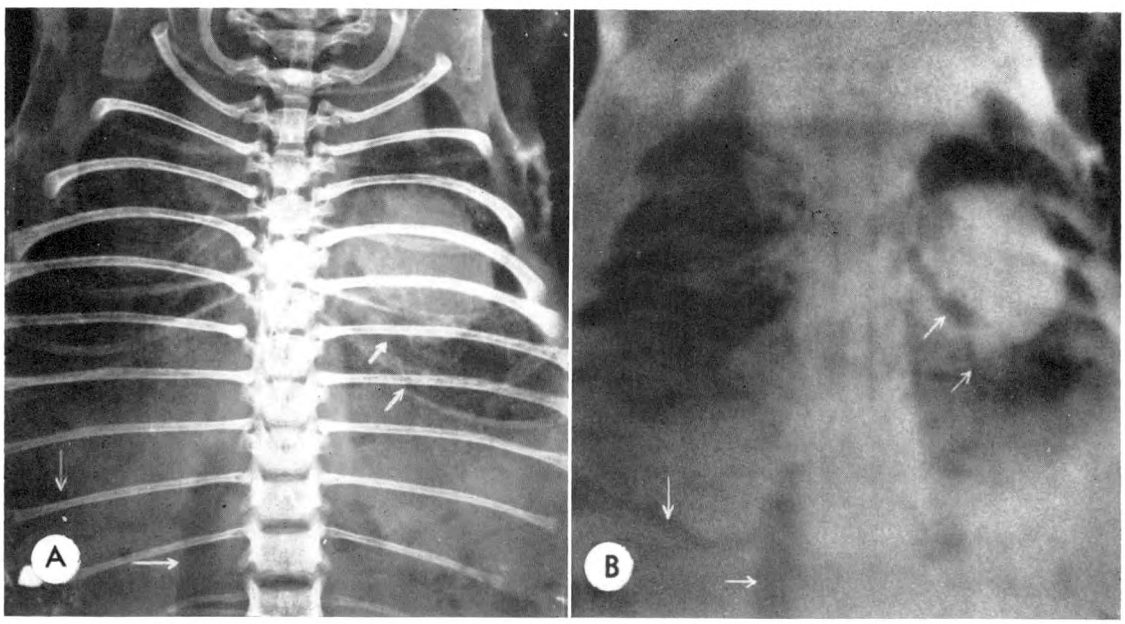


FIG. 2. Comparison of (*A*) 15 kvp. roentgenogram and (*B*) thermal neutron radiograph of a piece of round steak 1 cm. thick. Note that the bone is radiolucent to neutrons. The fat-muscle contrast is lost in the neutron radiograph, but the fat-air contrast is enhanced. The elastic scattering of neutrons from the hydrogen nucleus is primarily responsible for the attenuation of neutrons in tissue, whereas the absorption and scattering of x rays in heavier elements dominate the photon attenuation. Thus, while hydrogen rich fat yields maximum neutron attenuation, minimum photon attenuation is observed. The reverse occurs in hydrogen deficient bone.



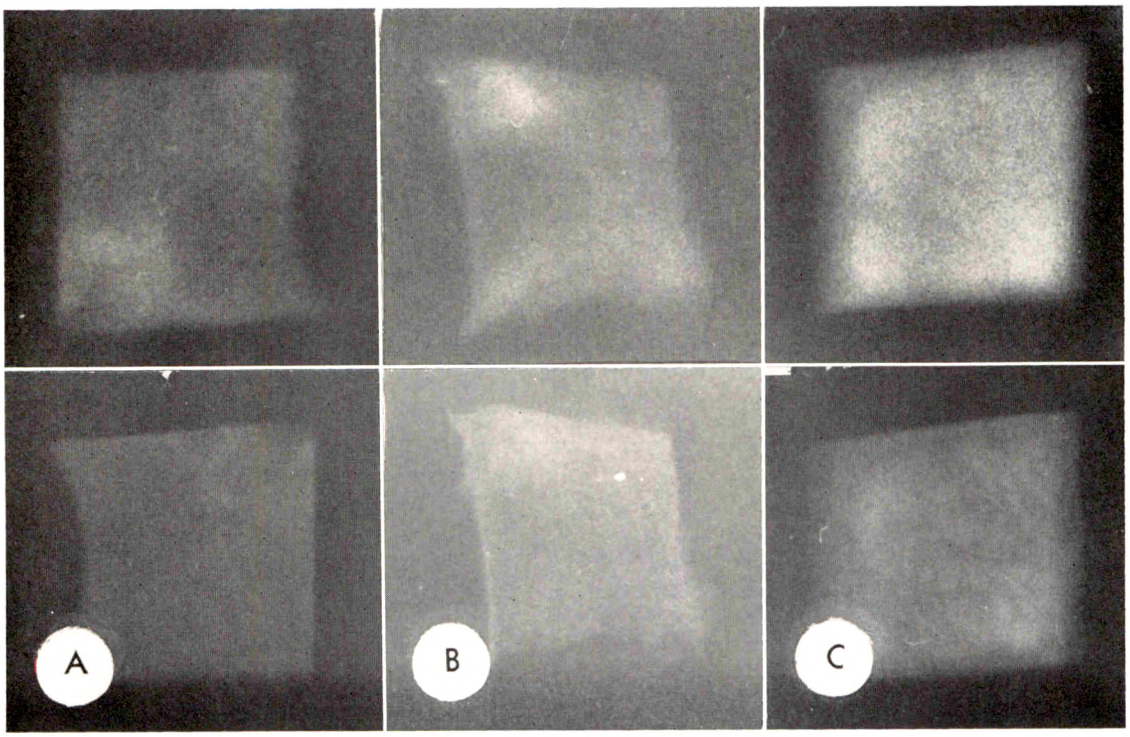


Fig. 4. Tumor specimen radiographs. (*A*) Adenocarcinoma. (*B*) Liposarcoma. (*C*) Leiomyoma. The thermal neutron radiographs are displayed in the upper row. The control 20 kvp. roentgenograms for each tumor lie immediately below. The reason for the greater contrasts seen in the neutron radiographs remains obscure, but is probably related to differences in hydrogen density. Frigerio has observed that many tumors have a higher hydrogen content than normal tissues.[5]

was used to preserve as much of the available information on the original films as possible. The experimental conditions of the neutron radiographs and roentgenograms are summarized in Table 1.

Pertinent observations from the neutron radiographs and roentgenograms are detailed in the legend of each figure.

Comparison of the low energy neutron radiographs and roentgenograms in Figures 2 to 8 resulted in several general observations which may be summarized as follows:

1. Interference from overlying bone shadows was eliminated in the neutron studies.
2. The negative contrast agents, air and heavy water, showed significantly better contrast in tissue when low energy neutrons were used.
3. The positive contrast agents, gadolinium and indium, were better vis-

←

Fig. 3. Comparison radiographs of the compressed chest of a dead rat. (*A*) High definition, low kvp. roentgenogram. (*B*) Neutron radiograph (0.025 ev.). The neutron radiograph demonstrates enhancement of the contrast between the air and soft tissues. Note also that the shadows of the overlying bone have disappeared. Air in the pulmonary arteries (↗) as well as within the hepatic vein (↓) and vena cava (→) can be much better visualized in the neutron radiograph. Compression of the chest was necessary because a tissue thickness of one inch is the practical limit of slow neutron techniques.

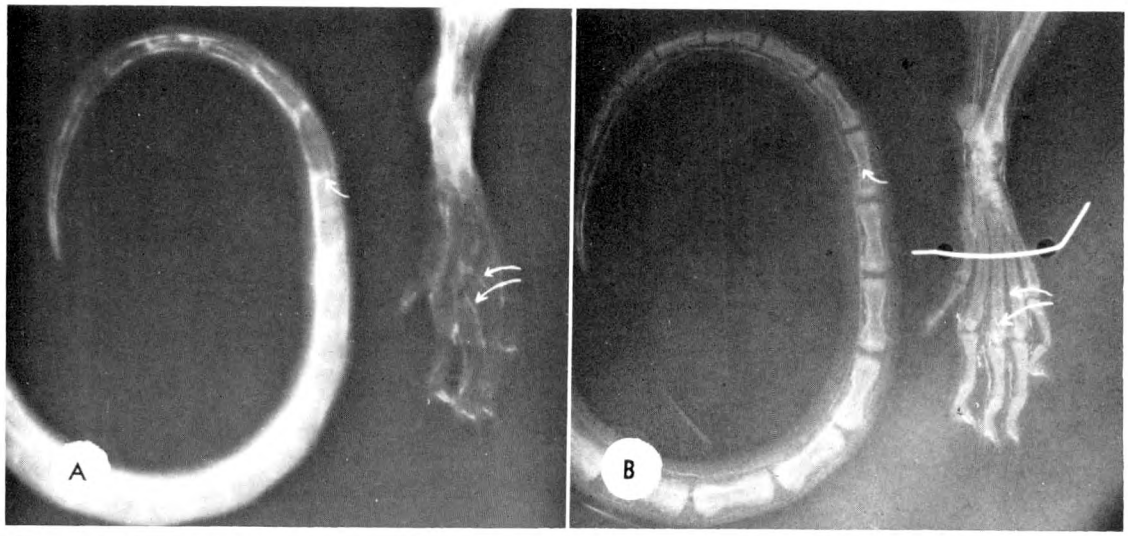


FIG. 5. Neutron arteriography. (*A*) Thermal neutron radiograph of a rat paw and tail. (*B*) Conventional nonscreen roentgenogram. Gd_2O_3 in oil was the contrast agent. The superior definition on the roentgenogram is compensated for by the complete absence of any bone shadow interference in the neutron radiograph. Note that in several areas the arteries are better visualized on the neutron radiograph than on the conventional roentgenogram (arrows).

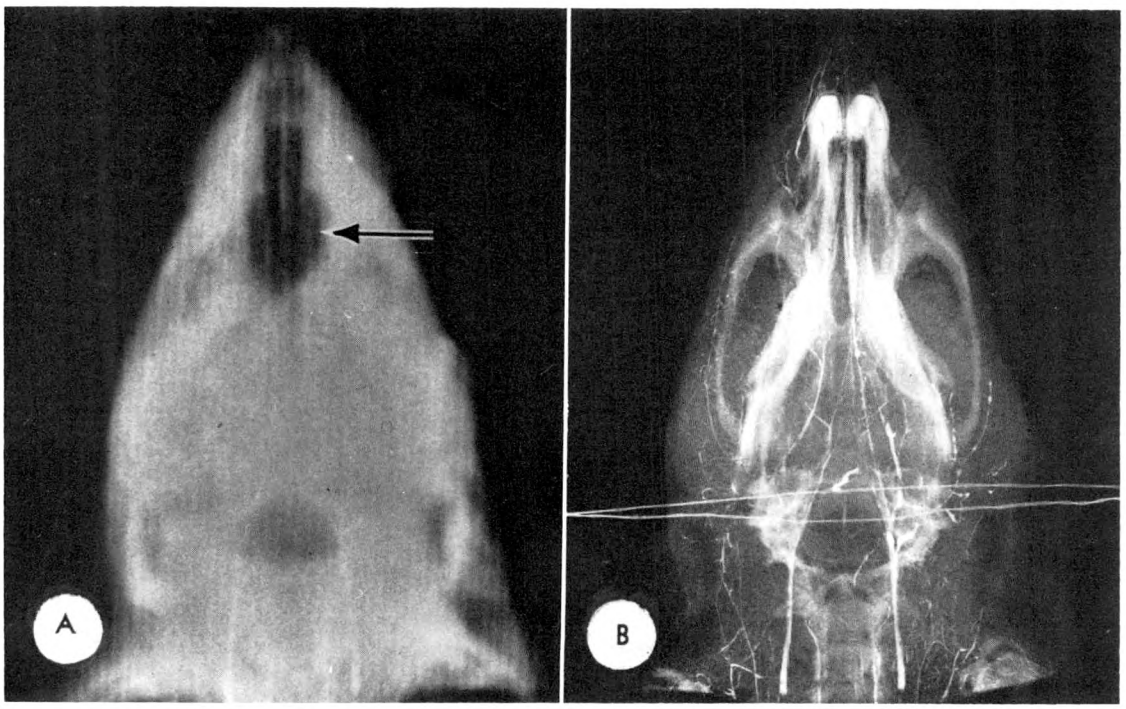


FIG. 6. Carotid neutron arteriography. (*A*) Epithermal neutron radiograph. (*B*) Conventional nonscreen roentgenogram. Although the epithermal beam was too weak to demonstrate the In_2O_3 contrast agent intracranially, the negative contrast areas are well seen. The excellent visualization of the nasopharynx (←) with neutrons is due to improved air contrast and the absence of interfering osseous shadows.

ualized in the tissue studies when conventional roentgenographic techniques were used (except where overlying bone interfered).

4. The effectiveness of the positive contrast agents could be changed markedly by changing the energy range of the neutrons detected.
5. The maximum tissue penetration for useful radiographs was about 2.5 cm. when low energy neutrons were used.
6. Line definition was significantly compromised in the neutron studies by the large dimension of the neutron emitting surface within the reactor core.

The elimination of the interfering bone shadows in the neutron studies follows simply from the relatively low hydrogen content of osseous structures. The improved visualization of air is caused by the difference in mean free paths of the neutron and x-ray beams. The air contrasts with neutron and x-ray beams, which have the same mean free paths in tissue, should be identical. The mean free path of conventional x-rays is, however, considerably longer than that of low energy neutrons. The visualization of heavy water, on the other hand, is a significant observation and may have important *in vivo* applications.

Neutron imaging techniques should at least be capable of definition comparable to that of conventional roentgen techniques using converter screens. All of the neutron radiographs of this report suffer from excessive geometric unsharpness. This is an inherent problem in using a large neutron emitting surface. Most x-ray tubes have an x-ray emitting surface (focal spot) which has a maximum dimension of 0.3 to 2.0 mm. The "effective focal spot" of the SP reactor was approximately 76 mm.

Three methods of reducing the geometric unsharpness associated with an excessively large emitting surface (assuming the object to recording surface has been minimized) are: (1) to increase the distance between the source and sample; (2) to use a diverging collimator that arbitrarily limits the source dimension; or (3) to use a series of parallel small diameter collimators.[6,10] The relatively low neutron output of the SP reactor precluded the use of any of these methods, but they can be employed on higher source strength reactors.

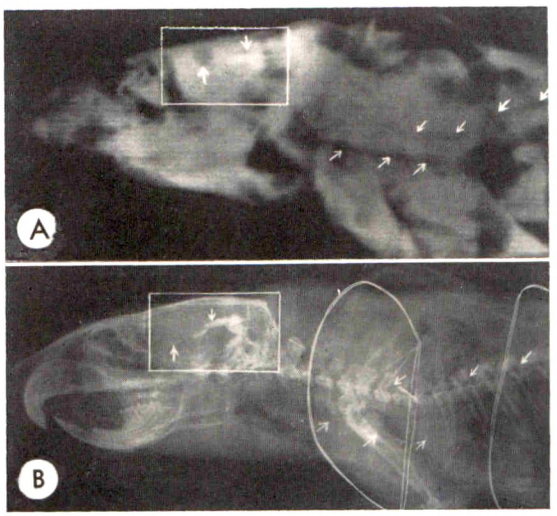


Fig. 7. Neutron ventriculography. (*A*) Thermal neutron radiograph. (*B*) Conventional nonscreen roentgenogram. Air and Gd_2O_3 were introduced by cisternal puncture. Note the superior visualization of the air in the ventricle (↑), trachea (↗), and spinal canal (↙) in the neutron study.

PHYSICS OF LOW ENERGY NEUTRON RADIOGRAPHY IN TISSUE

REACTOR NEUTRON SPECTRUM

A typical extracted neutron spectrum from a reactor may be conveniently divided into three adjoining energy regions: thermal, epithermal, and fast. The fast and epithermal regions include the fission born neutrons (approximately 2 mev. average energy) and a broad continuous spectrum of partially moderated neutrons down to about 0.5 ev. There is no natural boundary between the fast and epithermal regions, but for radiographic purposes 100 ev. could be considered a convenient conceptual boundary. Below 0.5 ev., the thermal spectrum is usually strongly peaked and is similar to that of a gas in kinetic equilibrium.[15] This distribution has a peak at

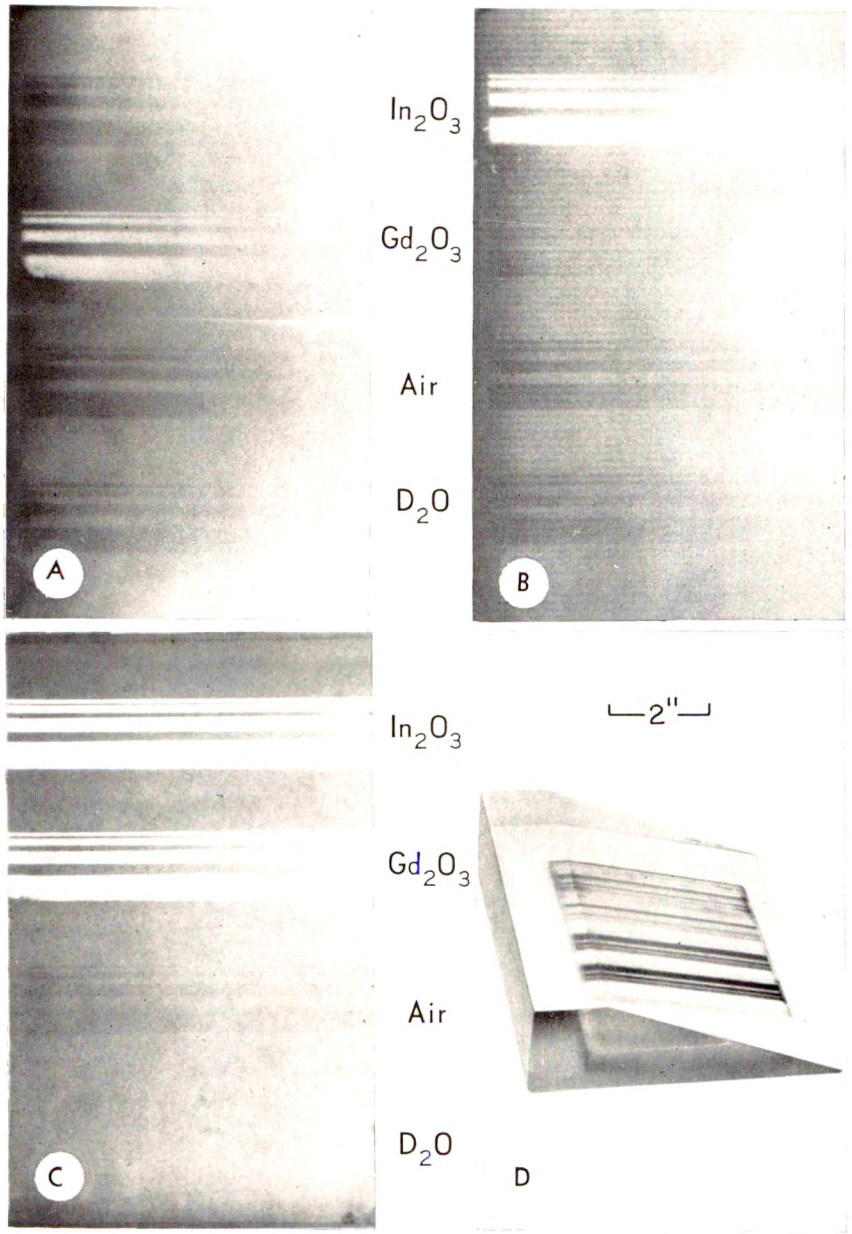


FIG. 8. Tissue substitute test wedge. (*A*) Thermal neutrons. (*B*) Epithermal neutrons. (*C*) 45 kvp. x rays. (*D*) "Lucite" test wedge. Two positive contrast agents (In_2O_3 and Gd_2O_3) and two negative contrast agents (air and heavy water) are displayed as 1/16 inch thick line pair phantoms (8, 16, and 32 L.P./I.) in the lucite test wedge. Note the improved contrast of the air shadows and the visualization of heavy water when neutrons are used. Note also the pronounced difference in the contrast offered by gadolinium and indium at the two neutron energies.

about 0.025 ev. for room temperature moderators such as the graphite of the SP reactor.

The relative magnitude of the thermal and the epithermal portions of the low energy neutron spectrum varies between different reactor facilities. The images from the two portions of the beam can be effectively separated by filtration or by selective imaging techniques.

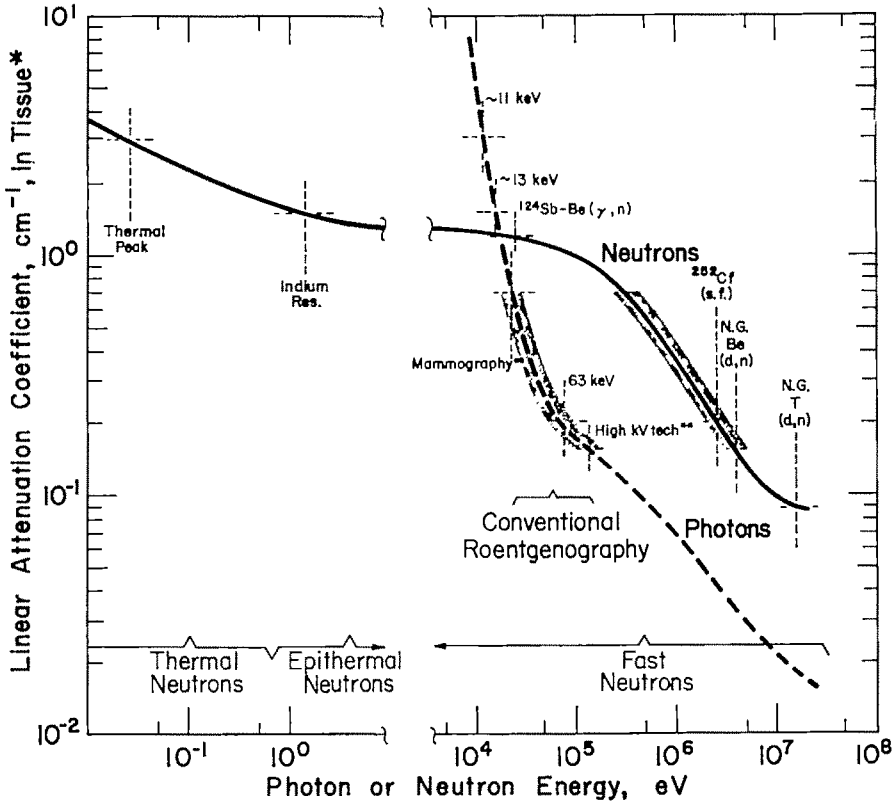


FIG. 9. Comparison of x- or γ-ray attenuation with neutron attenuation in tissue. Note that the penetration obtainable with conventional x rays can be duplicated only with fast neutrons. Neutrons from Cf^{252} will be similar to 63 kev. x rays in average tissue penetrability. The penetrability of thermal neutrons can be compared to 11 kev. x rays and epithermal neutrons to 13 kev. x rays.
* Homogenized standard man tissue.[19] Density = 1.0 gm./cm.³.
** M.C.G. routines (20–150 kvp.).

PENETRATION

Neutron radiographic images, like photon images, are the result of local variations in the attenuation of the impinging beam within the media. These variations are governed solely by the linear attenuation coefficients of the materials within the media and by the thickness of the contrasted media (exclusive of statistics).

The average attenuation in tissue of photons is compared to that of neutrons as a function of particle energy in Figure 9. The components of the "standard man"[19] have been homogenized and normalized with a whole body density of 1.0 gm./cm.³ to calculate average linear attenuation coefficients, μ_x and μ_n. In this comparison, all photoelectric absorption edges and resonance peaks have been smoothed over to simplify the display. Below 10 ev., Barton's[8] "bound atom" calculated values are used to normalize the neutron variation. These data show that low energy neutron radiography will probably be restricted to thin tissues (<2.5 cm.). Radiography of much greater tissue thicknesses will almost certainly require the greater penetration that can be obtained in the fast neutron region.

CONTRAST

Low energy neutron radiographs of biologic tissue have contrast principally because the density of hydrogen differs in various parts of the sample. The interaction probability of a neutron with a hy-

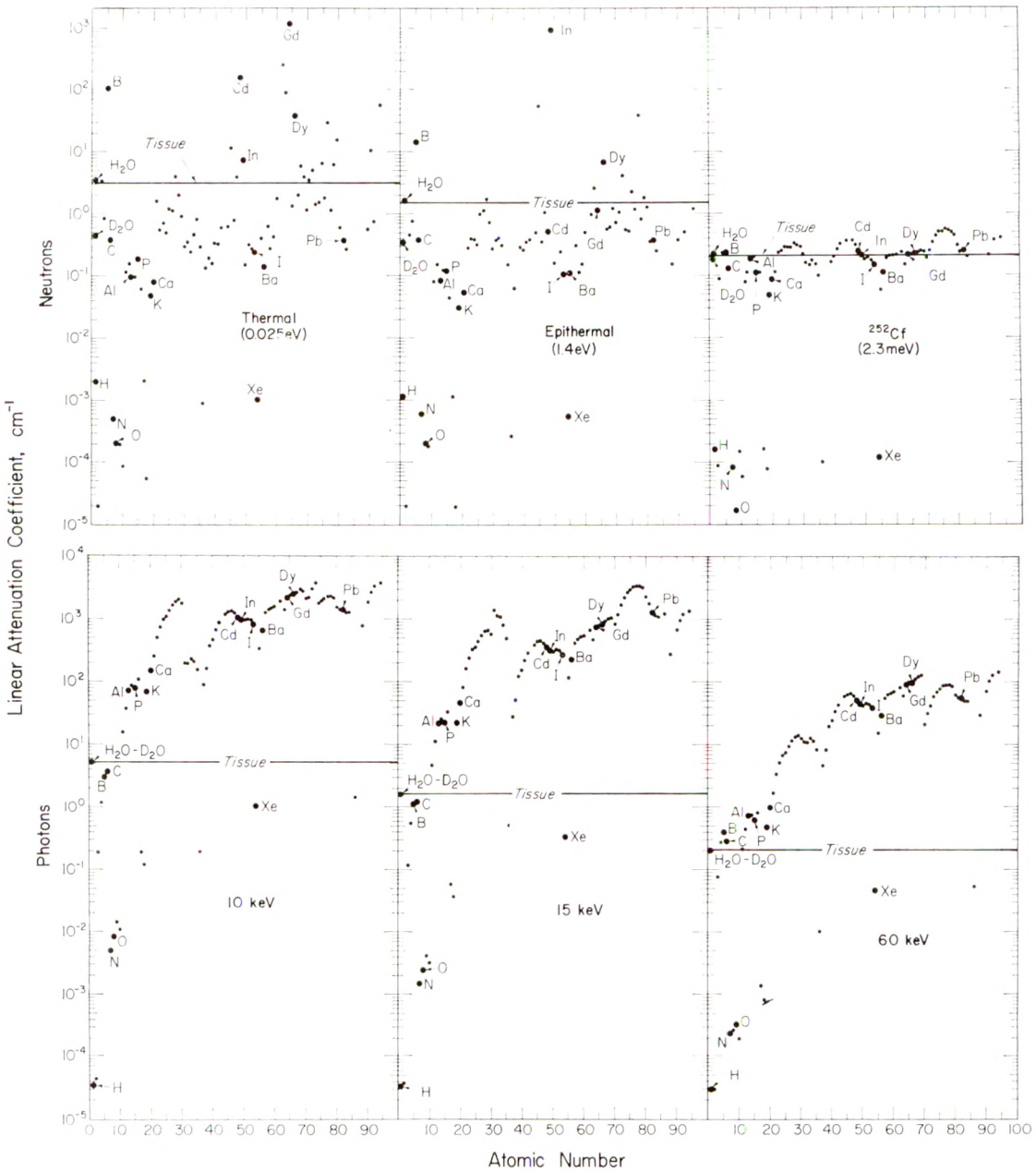


FIG. 10. Comparison of neutron and photon linear attenuation coefficients of natural elements (and light and heavy water) *vs.* standard man tissue.[19] These particular photon energies were chosen since such photons have nearly the same penetrability through tissue as the above neutrons. Prominent thermal positive contrast agents are boron, cadmium, gadolinium, etc.; prominent negative contrast agents are D_2O (heavy water), air, noble gases, calcium, barium, etc.

drogen nucleus is much larger than with other nuclei, and, furthermore, the hydrogen density is large. In "standard man" tissue, approximately 94 per cent of all thermal neutron interactions are elastic scattering from hydrogen. On the other hand, in roentgenography the heavier elements attenuate the photons much more than does hydrogen.

To choose agents to artificially enhance

contrasts in neutron radiographs, the attenuation coefficients of the various elements must be known. Figure 10 compares the linear attenuation coefficients of the elements with those of tissue ("standard man"[19]) and light and heavy water[18,16] at selected energy levels (0.025 ev., 1.4 ev., and 2.3 mev.—average thermal energy, the indium resonance peak, and the average energy of neutrons from Cf^{252}, respectively). A similar display of linear attenuation coefficients for x-ray photons having energy levels selected to yield a nearly equal ability to penetrate tissue ("standard man"[19]) have been shown for comparison (10, 15, and 60 kev., the energy levels having the nearest comparable mean free path for which data were available[23]). The attenuation coefficients (or macroscopic cross-sections) are for the natural form of these elements. The neutron data can be used to estimate the contrasts attainable with neutron beams approximating these energies.[7]

To induce maximum negative contrasts artificially, displacement of tissue or fluid with a substance of a very low attenuation coefficient is needed. From Figure 10 it is obvious that any gas can be used to approximate this condition. Similarly, D_2O (heavy water) is effectively transparent to slow neutrons.

To induce positive contrast artificially, strong neutron absorbers should be introduced into the tissue medium. For thermal neutron radiography, boron, cadmium, samarium, europium, and gadolinium are the best substances if maximum contrast is the only criterion. Many individual isotopes of various elements have much higher macroscopic cross-sections. For example, Gd^{157} has an absorption cross-section of 7,320 $cm.^{-1}$ in the metallic form. An organic substance dilutely tagged with Gd^{157} might make a relatively nontoxic positive contrast agent.

Figure 10 also demonstrates why the use of thermal neutron radiography is spreading in industry. The pronounced differences in attenuation among the heavy metals make thermal neutron radiography quite useful for industrial purposes. However, the relatively high attenuation coefficient of tissue limits somewhat the potential for artificially inducing positive contrast. In biologic media, it is usually easier to image an induced negative contrast.

Positive contrast elements are usually injected into a sample in a dilute mixture with some liquid carrier. Thus, the contrast agent has a much smaller cross-section than that of the pure element. The resulting positive contrast is proportional to μ (agent)—μ (tissue), which is apt to be small. The symbol μ is for the macroscopic cross-section ($cm.^{-1}$). On the other hand, the negative contrast from displacing soft tissue with a gas is more nearly proportional to the relatively high cross-section of the tissue alone. Therefore, for low energy neutron radiography, the absolute value of the possible positive contrast is often less than the absolute value of the negative contrast induced by gases. In conventional roentgenography, this effect is usually reversed because the cross-section for conventional x rays in tissue is much lower.

FAST NEUTRON RADIOGRAPHY

The data of Figure 9 show that fast neutrons will be necessary to penetrate most parts of the human body. Medical radiography demands both minimal patient exposure to radiation and relatively short exposure times; thus, both efficient image visualization systems and intense fast neutron sources are necessary. Efforts to develop efficient visualization systems and antiscatter techniques are currently underway.

For a given dose, fast neutrons are inherently at a statistical disadvantage when compared to x-ray photons in the conventional range. Clinical applications will be warranted only if the information gained justifies the increased dose or if less spatial resolution proves to be acceptable. These judgments will probably have to await

trials with a working fast neutron radiographic facility.

Sufficiently intense sources of fast neutrons are now available. Small accelerators (neutron generators) can provide an intensity of 10^{11} n/sec. The same intensity could be obtained with about 42 mg. of the radioactive isotope Cf^{252}, and could be concentrated to approximate a point source. Costs are expected to be competitive when this isotope becomes more readily available.[20,22]

The general character of a fast neutron image produced with a Cf^{252} source (average neutron energy = 2.3 mev.) can be predicted from published cross-section data. In general, fat, muscle, and bone will all have very similar attenuation coefficients and will thus not be particularly distinguishable. As in low energy neutron radiography, hydrogen will dominate the contrast (at 2.3 mev., 88 per cent of the neutron attenuation in "standard man" is due to elastic scattering from hydrogen). To the extent that certain tumors contain more hydrogen than adjacent tissues, it may be anticipated that their contrast will be enhanced. Figure 10 also shows that gaseous negative contrast agents will be far more effective than positive contrast agents.

CONCLUSIONS AND SUMMARY

Neutron radiographic techniques were studied to determine their applicability to the visualization of biologic structures. Conventional roentgenograms and low energy neutron radiographs of various biologic specimens were compared. The radiographic densities observed were noted to be significantly different. Bone was found to be radiolucent when using neutrons. Fat and muscle could not be differentiated; however, air contrasts were enhanced in the neutron studies. The use of heavy water and gaseous compounds to artificially induce tissue contrasts appears to be the most promising area of investigation in low energy neutron radiography.

Should fast neutron radiographic techniques be developed, they should be more useful where air must be visualized in the presence of bone and soft tissue. Preliminary dosimetry suggests that patient dose will not in itself preclude the clinical use of neutron beams for diagnostic purposes.

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X-RAY DENSITY CHANGES IN THE HUMAN HEEL DURING BED REST*

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ROENTGENOGRAPHIC densitometry has been used to estimate bone mineral losses during weightlessness of orbital space flight[2] and during anti-gravity simulation by extended bed rest of volunteer subjects.[3,4] Bone mass losses have been reported in both instances, with a greater magnitude of loss during actual weightlessness than in its bed rest simulation.

The computing apparatus used in these studies is capable of highly accurate measurements of changes in x-ray absorption by bone,[5,6] and it is probable that the reported changes in bone mass by the method of densitometry used reflect real variations in bone mineral or matrix. However, it is also possible that the observed changes were partly a consequence of changes in quality or quantity of surrounding soft tissues, which was an uncorrected variable in both the space flight and bed rest studies, *e.g.*, the tissue thickness at the os calcis site will vary as a result of the state of hydration, venous pooling, or changes in muscle mass.

Although the mass x-ray absorption coefficient by bone at 60 kv. is approximately 1.4 times greater than that of soft tissue (0.34 and 0.25, respectively), and the volume of overlying soft tissue is small in comparison with bone volume, it is probable that rather small changes in tissue mass are detectable roentgenographically. In fact, we have determined that a 10 per cent change in x-ray absorption will occur when the tissue thickness at the os calcis site is increased or decreased by 5 mm.

The effect of gravity on venous pooling and its effect upon roentgenographic density of the os calcis has been measured in a simple experiment (Fig. 1). Three successive roentgenograms were taken of an adult foot with the subject in the normal vertical position, and 3 roentgenograms were taken after the subject's leg had been elevated at a 45° angle for 15 minutes. It was found that the os calcis site in the elevated position absorbed 5 per cent less x-radiation than with the leg in the vertical position. It is apparent, therefore, that venous pooling in the extremities is an important factor to be considered in the interpretation of apparent bone density changes by x-ray densitometry.

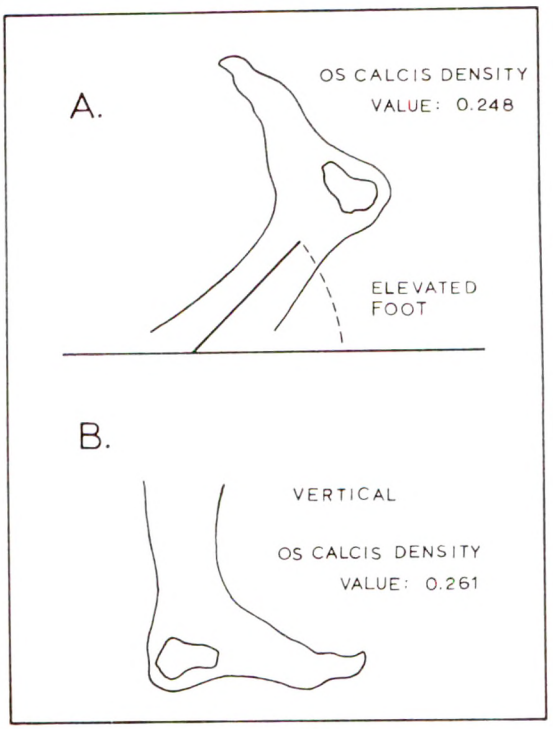


FIG. 1. (*A* and *B*) Variations in x-ray density of the os calcis as a result of venous pooling.

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MATERIAL AND METHOD

Four healthy young adult male volunteers participated in a bed rest study in which 3 subjects underwent complete recumbency for 14 days and 1 subject was retained as an ambulatory control. Efforts were made to duplicate as closely as possible the conditions reported in the other bed rest studies.[3,4]

Roentgenograms of the left foot and hand adjacent to an aluminum alloy calibration wedge were made at the same time each day. The same mobile x-ray unit was used throughout the study, and a standard absorber having a mass similar to that of the os calcis was roentgenographed daily to detect spurious variations which might contribute to erroneous density interpretation. Eastman Type AA fine grain x-ray film was used and double-loaded into cardboard exposure holders. One of the 2 films was developed immediately for quality check, and the second film was retained for the simultaneous development of all films at the termination of the study.

Exact reproducibility in alignment was accomplished by marking the center of the os calcis with a permanent dye target, and the foot was superimposed each day upon the photographic print of the subject's original roentgenogram (Fig. 2, *A* and *B*).

All roentgenograms were evaluated 2 times with the bone density computer at Texas Woman's University. If the values varied by less than 2 per cent, the average value was used. If a deviation greater than 2 per cent resulted, one or more additional evaluations were made. Routinely, the instrument can be expected to produce re-evaluations of a single roentgenogram well within the 2 per cent limit regardless of the time factor between evaluations.

Tissue thickness was measured by caliper at the dyed target site immediately prior to the x-ray exposure.

RESULTS AND DISCUSSION

All subjects exhibited rather marked daily variations in os calcis x-ray absorption throughout the study. Hegsted[1] has suggested that such short-term changes are a "normal biologic variable" and cautions that they may have no significance in reflecting real changes in bone density. However, when the os calcis aluminum equivalency values for the entire 2 week period were plotted and analyzed by the method of least squares (Fig. 3), a gradual increase in roentgenographic density occurred in the 3 bed rest subjects in contrast to no change in the control subject (who served as a daytime orderly).

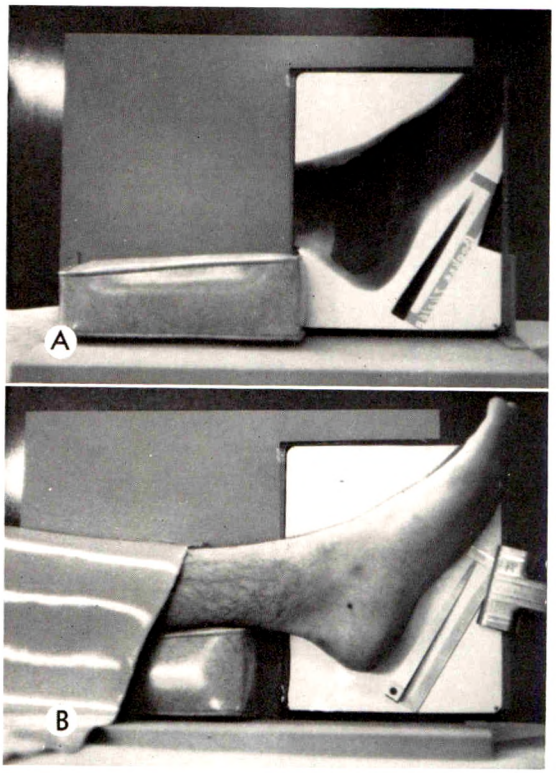


Fig. 2. (*A*) Footholder and aligning photograph used to assure reproducible x-ray positioning during os calcis densitometry. (*B*) Foot in position for densitometry.

The largest increase occurred in bed rest subject D.C. (7.2 per cent) followed by increases of 6.3 per cent and 5.7 per cent in subjects N.M. and T.B., respectively. The os calcis density change in control subject J.W. was less than 1 per cent. The correlation coefficients for each of the bed rest subjects were significant: subject D.C.: $P = 0.506$ ($r = 0.005$); subject N.M.: $P = 0.488$

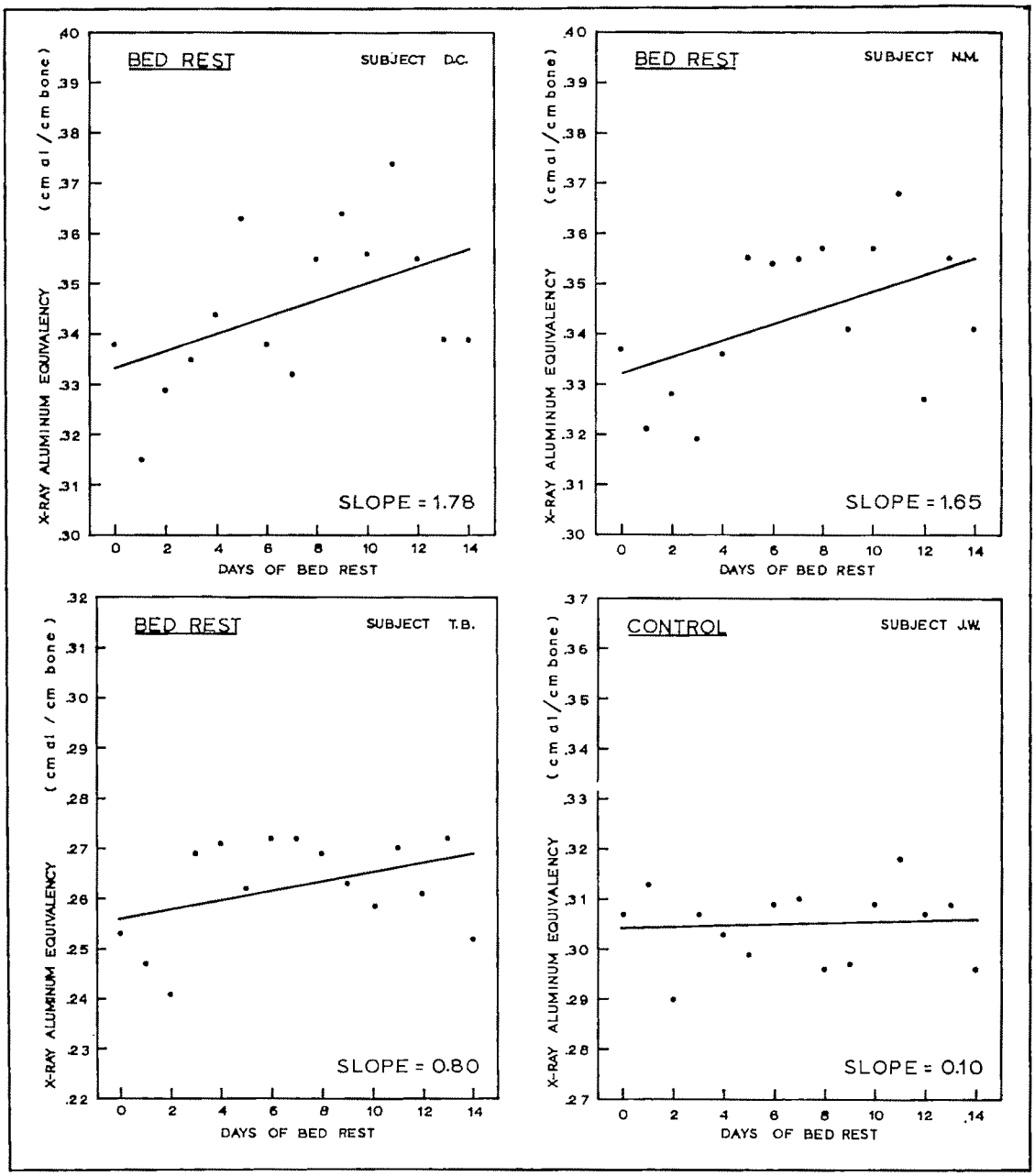


FIG. 3. Os calcis density patterns preceding and during bed rest for the 3 experimental subjects and 1 control subject.

(r=0.05); and subject T.B.: P=0.360 (r=0.10). The correlation coefficient, P, for control subject J. W. was 0.060 (r=N.S.). The slopes for the os calcis of all subjects are shown in Figure 3.

The second phalanx of the right hand and the distal epiphysis of the radius were analyzed in the same manner and no significant change occurred during the course of the study.

Caliper thicknesses at the os calcis site during early and final periods of bed rest (Days 1–3 and Days 13–14) indicated that the mean tissue thickness increased among

TABLE I

THICKNESS AT THE OS CALCIS SITE (BONE AND OVERLYING TISSUE) DURING THE FIRST 3 DAYS AND THE FINAL 2 DAYS OF THE STUDY

Subjects	Over-all Thickness at the Os Calcis Site (cm.)		Values of t	
	Days 1–3	Days 13–14	t	P
Bed Rest				
D.C.	5.43 (SD = .15)	5.90 (SD = .14)		
N.M.	5.33 (SD = .07)	5.60 (SD = .20)	2.53	.05
T.B.	5.50 (SD = .17)	5.70 (SD = 0)	(3 subjects)	
Control				
J.W.	5.13 (SD = .07)	5.10 (SD = c)	.767	NS

SD = standard deviation.
NS = not significant.

all 3 experimental subjects as the bed rest progressed, but there was no significant change in the control subject. The average tissue thickness for each subject and the t-test probability values between Days 1–3 and Days 13–14 are given in Table 1. The increases varied between 2 mm. and 6 mm. among the bed rest subjects, while the ambulant control subject, J. W., changed by only 0.3 mm. Since an increase or decrease in tissue thickness of 1 mm. will produce an x-ray absorption change of 2 per cent, the observed variations in tissue thickness could account for changes in x-ray absorption of 4 per cent to 12 per cent (and variations of this magnitude occurred during the study).

Some of the previous studies reported losses in x-ray density as a result of bed rest,[3,4] while the current study indicates that a slight gain occurred. In considering the magnitude of change in x-ray absorption observed in other studies (without regard to actual increase or decrease *per se*), it is important to notice that the changes in tissue thickness observed in the current study could readily explain the variations in bone density reported in the other studies involving bed rest—and reports of those studies do not indicate that tissue thickness was measured. In fact, the changes in tissue absorption which we observed could easily mask the slight changes in bone absorption normally expected to be associated with bed rest. For this reason, one must not conclude from *x-ray densitometry alone* that bone mass losses occurred in the earlier studies because the method of densitometry used did not differentiate between bone and tissue absorption.

It is obvious that an adequate soft tissue correction factor must be applied in future studies of the effects of bed rest and weightlessness upon skeletal density. A method now being used in this laboratory consists of encompassing both the body part and wedge in a tissue-simulating medium, lead shielding of the calibration wedge and body part from "undercut" scatter, and use of a scatter-reducing grid. This method has demonstrated greatly improved reproducibility in serial roentgenograms and higher precision in quantitating x-ray absorption to actual bone mineral content.

SUMMARY

In a study of the effects of recumbency on bone density, 3 young adult males participated in a study involving 14 days of complete bed rest, and 1 subject was retained as an ambulatory control.

A slight but significant increase in x-ray density at the os calcis site was noted among the bed rest subjects as the study progressed, but the increase was not evident in the control subject. No significant density variations occurred in the hand phalanx or distal radius.

Periodic caliper measurements of the heel indicated that increased tissue thickness during the latter phases of bed rest may have accounted for the apparent gain in x-ray density of the os calcis. Such an increase in tissue thickness may be a result of venous pooling in the limbs with immobilization.

An adequate soft tissue correction factor must be applied in future studies of the effects of bed rest and weightlessness upon skeletal density.

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VOL. 106, No. 3

SUPERIOR MARGINAL RIB DEFECTS*

AN ETIOLOGIC CLASSIFICATION

By E. NICHOLAS SARGENT, M.D., A. FRANKLIN TURNER, M.D., *and* GEORGE JACOBSON, M.D.
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THE occurrence of superior marginal rib defects has received little attention and has been infrequently reported as compared to inferior marginal erosions.[6,8,11,30,35,36] The conditions which have been associated with superior marginal rib erosions and defects are worthy of summarization and classification.

Throughout life, bone is laid down by the activity of osteoblasts and is absorbed by the osteoclasts. The two processes occur simultaneously and a dynamic equilibrium is established.[2,13,26] The causes of superior marginal rib erosion may be related to an osteoblastic-osteoclastic imbalance. Thus, the establishment of a useful classification based on deficient osteoblastic activity in contradistinction to excessive osteoclastic activity is possible (Table 1).

TABLE I

CLASSIFICATION OF SUPERIOR MARGINAL RIB DEFECTS

I. *Disturbance of Osteoblastic Activity* (decreased or deficient bone formation)
   1. Paralytic poliomyelitis (bulbar or spinal)
   2. Collagen diseases (rheumatoid arthritis, scleroderma, lupus erythematosus, Sjögren's disease)
   3. Localized pressure (rib retractors, chest tubes, multiple hereditary exostoses, neurofibromatosis, thoracic neuroblastoma, coarctation of the aorta with superior *and* inferior rib erosion)
   4. Osteogenesis imperfecta
   5. Marfan's syndrome
   6. Radiation damage

II. *Disturbance of Osteoclastic Activity* (increased bone resorption)
   1. Hyperparathyroidism
   2. Hypervitaminosis D (?)

III. *Idiopathic* (no demonstrable associated etiology)

I. DISTURBANCE OF OSTEOBLASTIC ACTIVITY

1. PARALYTIC POLIOMYELITIS

The occurrence of erosive rib lesions in patients with paralytic poliomyelitis has been well documented by Bernstein *et al.*[7] Rib changes did not occur earlier than 10 months after the onset of respiratory muscle paralysis, were most often seen after 20 months, and in one instance did not appear for 45 months. The rib lesions were unrelated to age, sex, type of therapy, or the presence of decubitus ulcer, and occurred in 14 of 28 patients requiring prolonged mechanical respiratory assistance. No clinical signs or symptoms were attributable to the rib involvement, however, the most severely paralyzed patients showed the greatest frequency of involvement.

The early involvement of the rib appeared as a localized shallow indentation with progressive narrowing of the upper cortical margins of the ribs, varying from 1 to 4 cm. in length. With progression, the rib cortex became successively thinner and there was associated localized osteoporosis with trabecular thinning of the involved rib segment. Occasionally a slight and similar indentation on the inferior cortical margin was seen with a consequent hourglass formation. In all instances the superior portion of the ribs was more severely affected.

Because of the localization of some rib lesions in areas directly contiguous to the medial margins of the scapula, it was felt that continued pressure of this area of the scapula against the ribs was the causative factor. The explanation offered was that bone destruction can be attributed to re-

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sorption, secondary to the application of a force to a bone surface area, normally not adapted to withstand pressure, particularly if applied in an abnormal direction.[34] A further mechanism offered was that pressure causes a primary change in the bone itself, leading to stimulation of osteoclastic activity and consequent loss of bone substance. The resorption of bone always progresses inward from the bone surfaces and never arises within the deeper layers of the bone structure.[23] However, these theories cannot explain why in 50 per cent of the completely immobile reported cases, rib changes did not occur. Furthermore, many ribs adjacent to the scapula were spared while other ribs at some distance away were involved.

Figure 1, *A* and *B* is an example of a patient with bulbospinal poliomyelitis who had been in a respirator for 16 years. There are typical erosions of the superior margins of the ribs localized to the third, fourth, and fifth ribs on the right and the fourth, fifth, and sixth ribs on the left. The erosions on the right are closer to the medial scapular margins and the erosions on the left are close to the lateral scapular margin. The right fifth rib also shows beginning inferior marginal rib erosion.

Aegerter and Kirkpatrick,[1] and Albright and Reifenstein[2,3] offer a more logical theoretic basis upon which one might explain the bone erosions. The "stress stimulus" is undoubtedly the most important of all the factors that govern conversion of coarse fiberbone to adult bone during normal skeletal growth, maintenance, and modeling. This is especially true during the replenishment of normal physiologic erosion of bone. Throughout the skeleton, mechanical stress stimuli are apparently necessary to convert primitive bone to the adult type. Without it, the lamellae remain unoriented and any minimal pressure causes distortion. The lack of the normal "stress stimulus" is well illustrated by comparison of a roentgenogram of a normal extremity bone with that of the same bone after it has been immobilized in a cast for several weeks. Postmortem examinations obtained of a few patients who died of long-standing bulbospinal poliomyelitis have shown complete loss of intercostal muscle fibers with replacement by a thin fibroadipose membrane in many of the intercostal spaces.[33]

Thus a more logical explanation of supe-

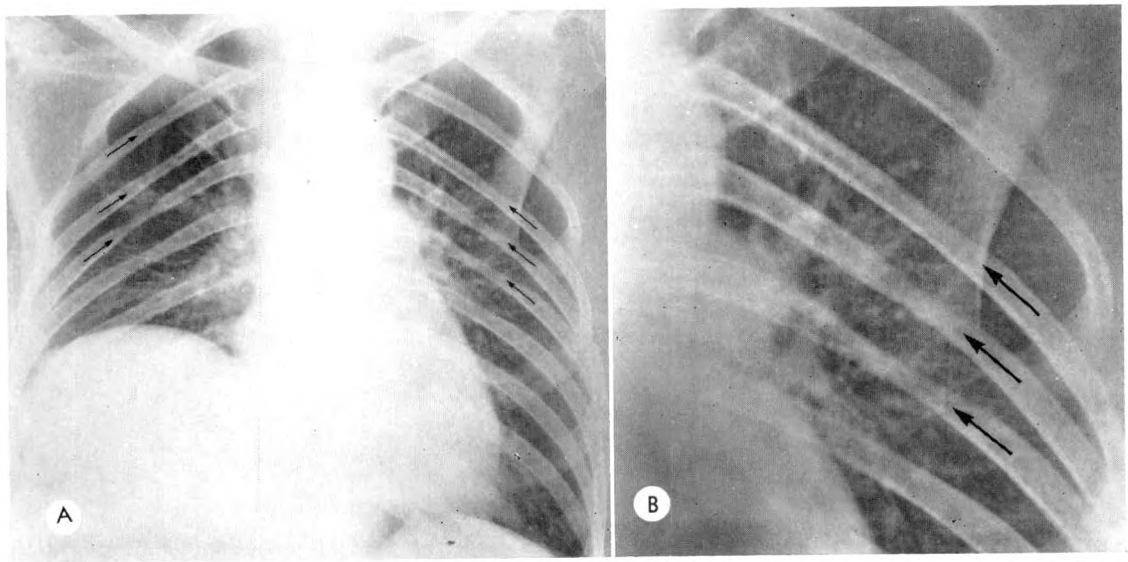


FIG. 1. (*A*) A 47 year old female with bulbospinal poliomyelitis who had been in a respirator continuously for 16 years. The vital capacity was 20 per cent of normal. Note the marginal defects involving the third, fourth, and fifth ribs on the right and fourth, fifth, and sixth ribs on the left. (*B*) Close-up view of typical posterior rib defects involving the fourth, fifth, and sixth ribs on the left.

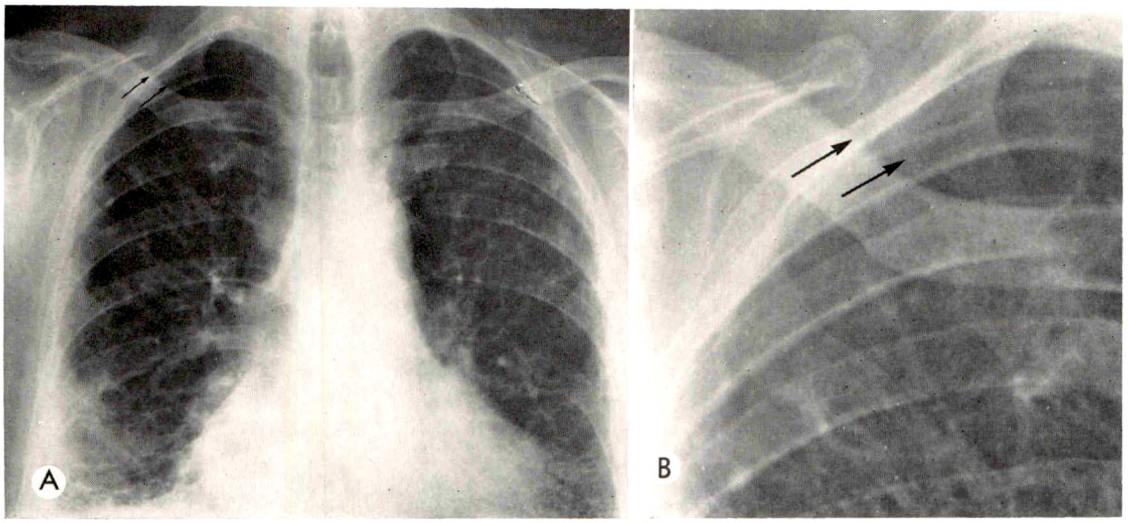


Fig. 2. (*A*) A 63 year old male with classical rheumatoid arthritis and rheumatoid pulmonary disease (proven by biopsy). There are superior marginal rib defects involving the second and third ribs on the right and the third rib posteriorly on the left. (*B*) Close-up view of second and third ribs on the right.

rior marginal rib erosions both adjacent to and distant from the scapula would therefore seem to be atrophy of intercostal muscles at their attachment to the ribs and their replacement by fat and fibrous tissue. This results in loss of the normal muscle pull, failure of the "stress stimulus" for normal osteoblastic bone production, and lack of replacement of osteoid which has been lost by physiologic erosion. Furthermore, the selectivity and extent of rib erosions might theoretically be related to the degree and extent of intercostal muscle fiber replacement, rather than due to any localized pressure phenomenon.

2. COLLAGEN DISEASES

(Rheumatoid Arthritis, Scleroderma, Lupus Erythematosus, Sjögren's Disease)

Martel and Duff[21] described 1 patient with bone absorption at the posterior ends of the ribs involving the costovertebral articulations. However, well delineated, notched rib lesions in 4 patients with advanced rheumatoid arthritis involving only the superior margin of the posterior aspect of the ribs were first described by Saint John Dixon.[29] Alpert and Feldman[4] have summarized the rib lesions of rheumatoid arthritis. These lesions were visualized as either localized areas of flattening or erosions. The changes were notably all confined to the superior borders of the posterior aspects of the third, fourth, and fifth ribs and did not involve the articular portions. One case described had complete destruction of a segment of the third rib mimicking malignant disease. When the lesions are small, they present as a cup-shaped excavation on the upper rib border. However, when larger, they also are manifested as a longer localized flattening of the superior contour. The lesions occurred in patients who did not receive steroids, so hyperadrenalism or hypercortisonism could not be implicated. Biopsies were not obtained to prove any replacement of osseous tissue by rheumatoid granulomas or by fibrotic residues of a rheumatoid inflammatory process.

Figure 2, *A* and *B* is an example of rib erosions in a patient with rheumatoid arthritis and rheumatoid pulmonary disease. Note the extensive superior marginal rib flattening in the second rib on the right and the more localized defects in the posterior aspects of the third ribs bilaterally.

Keats[16] described a patient with classic scleroderma and progressive bilateral superior marginal rib erosions involving the right fourth through the ninth ribs and the left third through the seventh ribs. Figure

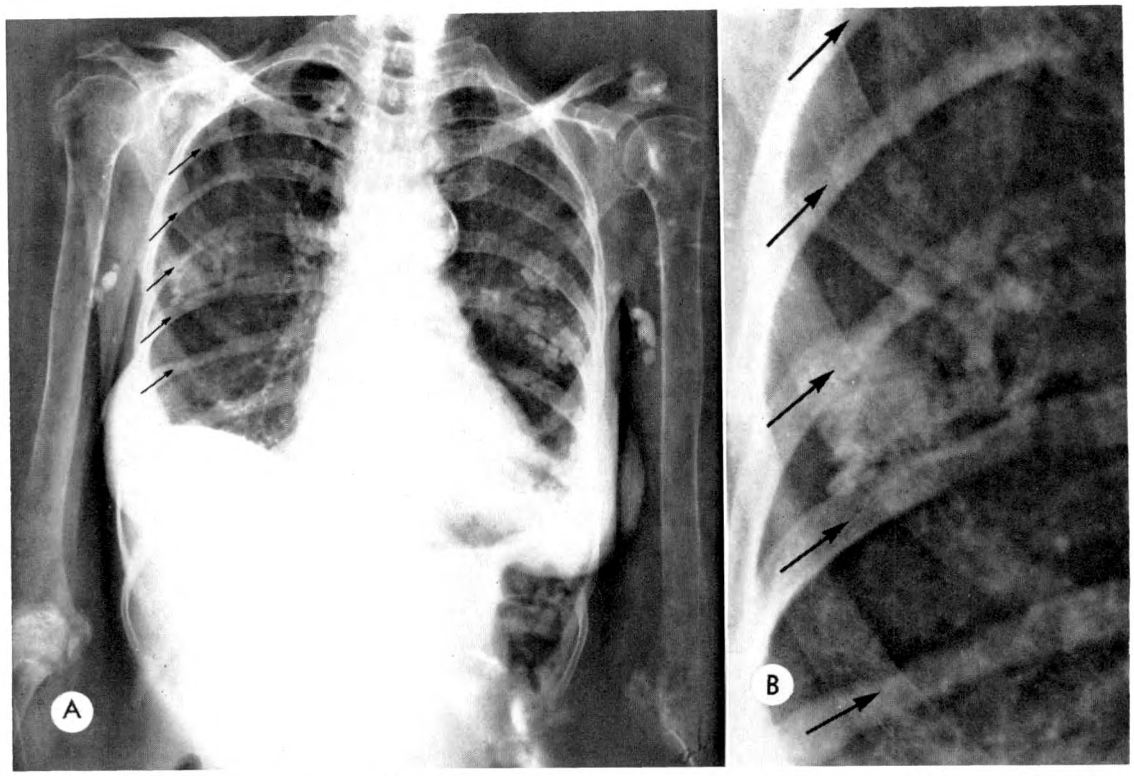


FIG. 3. (*A*) A 47 year old female with advanced systemic scleroderma and extensive soft tissue calcifications in the subcutaneous tissues of the extremities and body wall, associated with tumoral calcinosis. There are multiple superior marginal rib defects on the right. (*B*) Close-up view of upper right ribs. Several defects can be seen close to the scapula as well as some distance away.

3, *A* and *B* is an example of superior rib erosions seen in a patient with systemic scleroderma. Note the extensive defects in the posterior superior aspects of several ribs. Figure 4, *A* and *B* shows complete bilateral posterior rib destruction in another patient with progressive systemic scleroderma.

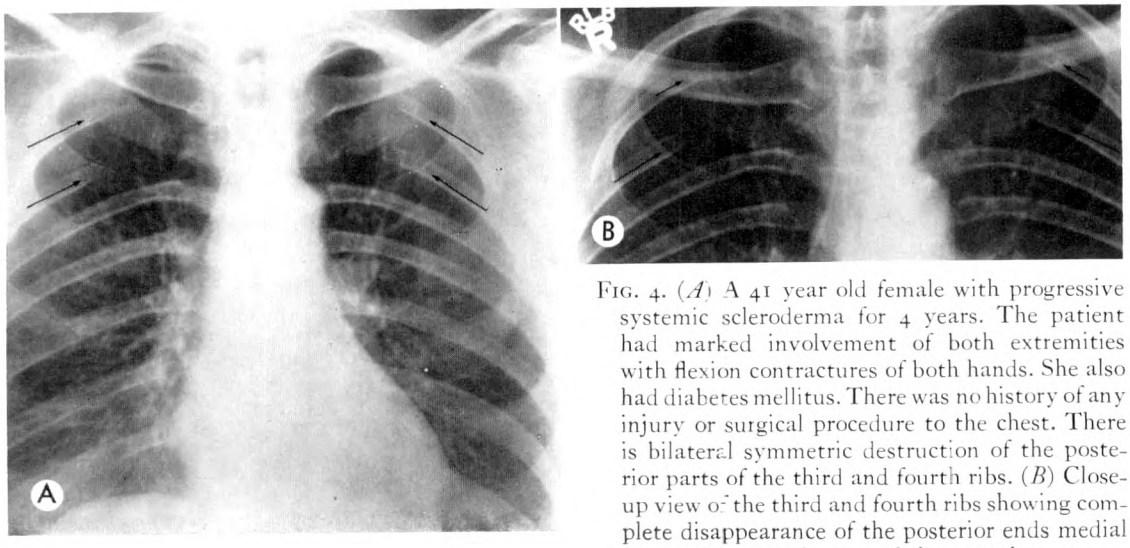


FIG. 4. (*A*) A 41 year old female with progressive systemic scleroderma for 4 years. The patient had marked involvement of both extremities with flexion contractures of both hands. She also had diabetes mellitus. There was no history of any injury or surgical procedure to the chest. There is bilateral symmetric destruction of the posterior parts of the third and fourth ribs. (*B*) Close-up view of the third and fourth ribs showing complete disappearance of the posterior ends medial to the vertebral border of the scapula.

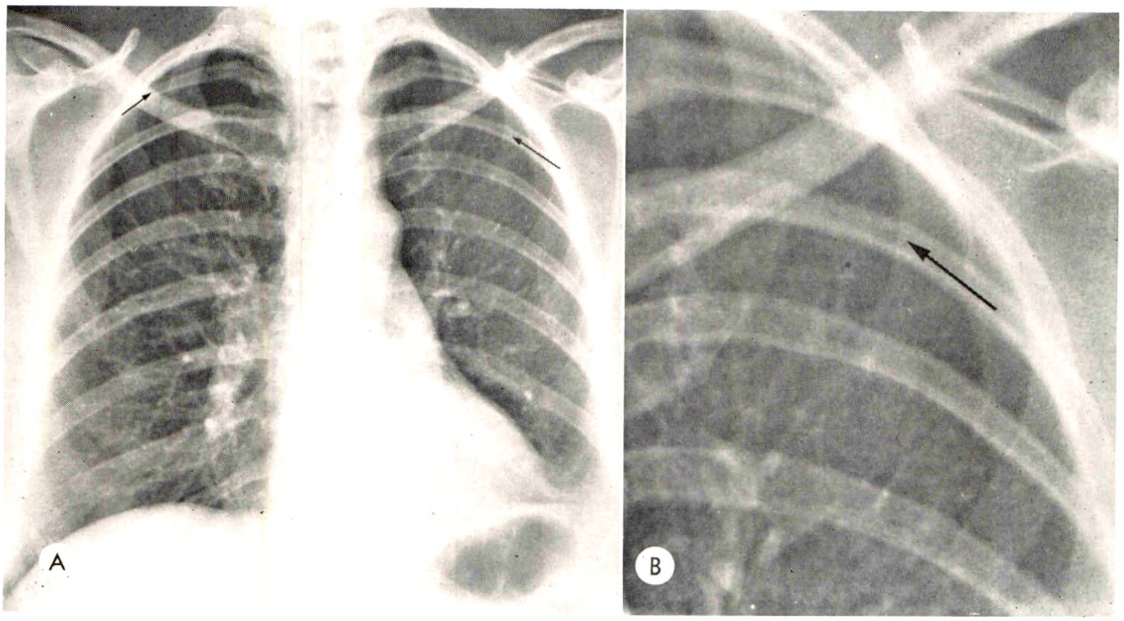


Fig. 5. (*A*) A 37 year old female with a discoid lupus erythematosus lesion on the nasal bridge and right cheek. There was intermittent arthralgia of the hands and bursitis of both knees. A diagnosis of typical subacute systemic lupus erythematosus was made clinically. (*B*) Close-up view of left upper chest showing shallow superior marginal rib defect involving the fourth rib.

Figure 5, *A* and *B* is an example of defects involving the left fourth rib and right third rib in a patient with systemic lupus erythematosus.

Figure 6, *A* and *B* shows rib erosions in a patient with Sjögren's syndrome associated with arthritis mutilans. Note the involvement of the third, fourth, and fifth ribs on the right. Smaller erosions are also seen on the left.

The superior marginal rib erosions and defects found with collagen diseases and paralytic poliomyelitis are essentially the same in appearance. Rapid atrophy of skeletal muscle; infiltration of follicles of lymphocytes throughout the muscle fibers

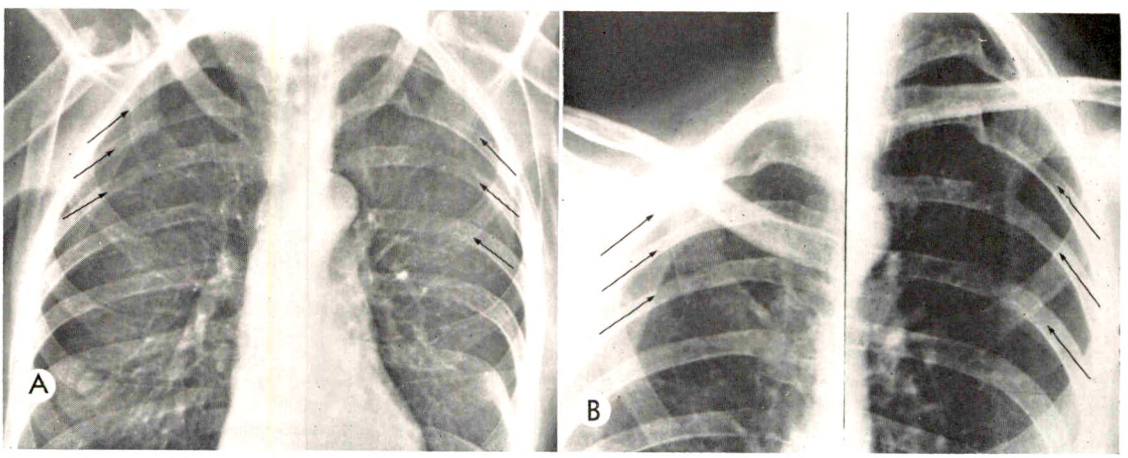


Fig. 6. (*A*) A 38 year old white female with an 18 year history of "rheumatoid arthritis." The patient had not been on steroid therapy for the past 15 years. There were also associated findings of Sjögren's sicca syndrome. (*B*) Close-up views of the right and left upper thorax showing bilateral superior marginal rib erosions (independent of areas due to old rib fractures).

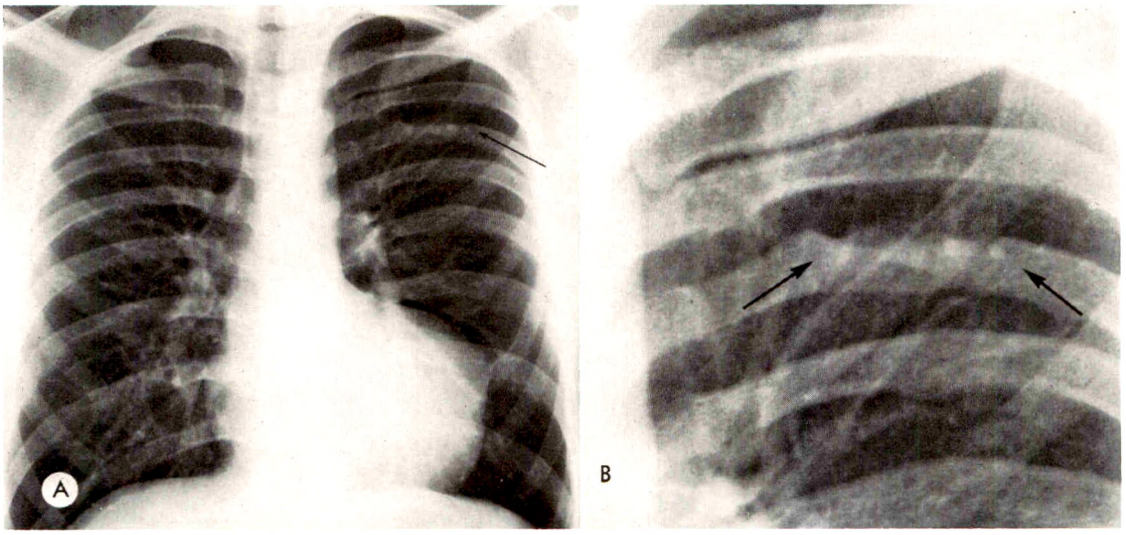


FIG. 7. (*A*) A 20 year old male with history of cardiac surgery for congenital heart disease. A recent cardiac catheterization showed aortic stenosis, left ventricular hypertrophy, and coronary insufficiency. Note the defect at the superior posterior margin of the fifth rib on the left following the use of rib retractors at this site. (*B*) Close-up view.

unrelated to joint involvement; and similarity of exudative inflammatory reactions occur with all collagen diseases. Localized loss of normal muscle stimulation required to convert primitive bone to the normal adult type for replenishment during physiologic erosions may, in the final analysis, explain the pathogenesis in all instances.

3. LOCALIZED PRESSURE EFFECT

Rib notching due to localized pressure may occur following the use of rib retractors during surgery and the use of intercostal chest drainage tubes. Figure 7, *A* and *B* shows loss of the superior margin of a rib following the use of rib retractors during an operation for congenital heart disease.

Both superior and inferior marginal rib defects have been found in patients with multiple hereditary exostoses, as shown in Figure 8, *A* and *B*. Although pressure from contiguous exostoses may explain some of the findings, the occurrence of defects unrelated to adjacent exostoses needs further explanation. Larger exostoses occurring at some distance from the localized defects may interfere with rib movements, thus eliminating the normal localized muscle pull stimulus to bone formation. Furthermore, the possibility of an associated congenital bone dysplasia with abnormal or deficient osteoid formation may also be an unrecognized factor.

Coarctation of the aorta with both superior and inferior rib erosion has been described by Sloan and Cooley[31] in 3 cases resulting from tortuous intercostal arteries extending down to and actually eroding the superior borders of the adjacent inferior ribs.

Thoracic neuroblastomas[28] often obscure the spine and ribs on routine chest roentgenography, yet the adjacent ribs are actually narrowed and eroded by the tumor. These changes are often more readily recognizable after a course of therapy and following tumor regression. Later the ribs may remodel, which is a good indication of arrest of tumor growth. Figure 9, *A* and *B* illustrates a thoracic neuroblastoma, with several of the posterior ribs on the left showing superior and inferior marginal erosions. The erosions disappeared as the tumor responded to radiation therapy.

Both superior and inferior marginal rib defects are often found in neurofibromatosis. Ribs arising from the abnormal verte-

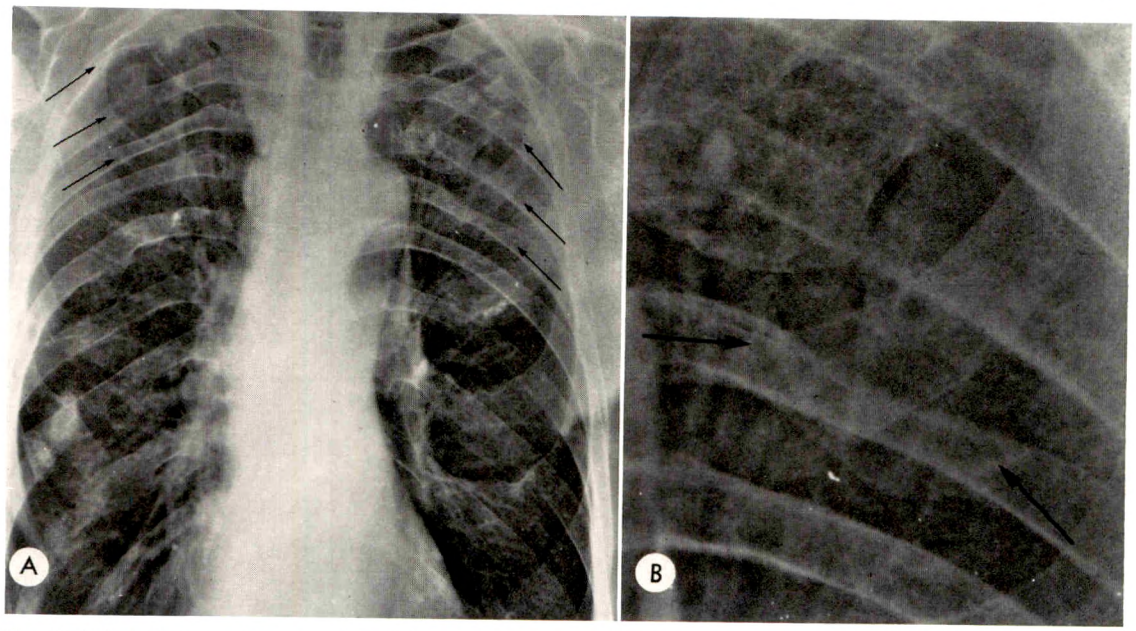


Fig. 8. (*A*) A 68 year old male with a history of many operations for removal of exostoses. He was clinically found to have involvement of all extremities and the thorax. Multiple superior marginal rib defects are to be noted adjacent to exostoses. However, several of the defects are found to be in areas unrelated to exostoses. (*B*) Close-up view of the sixth rib posteriorly on the left showing a typical scalloped elongated marginal defect with no evidence of adjacent exostosis.

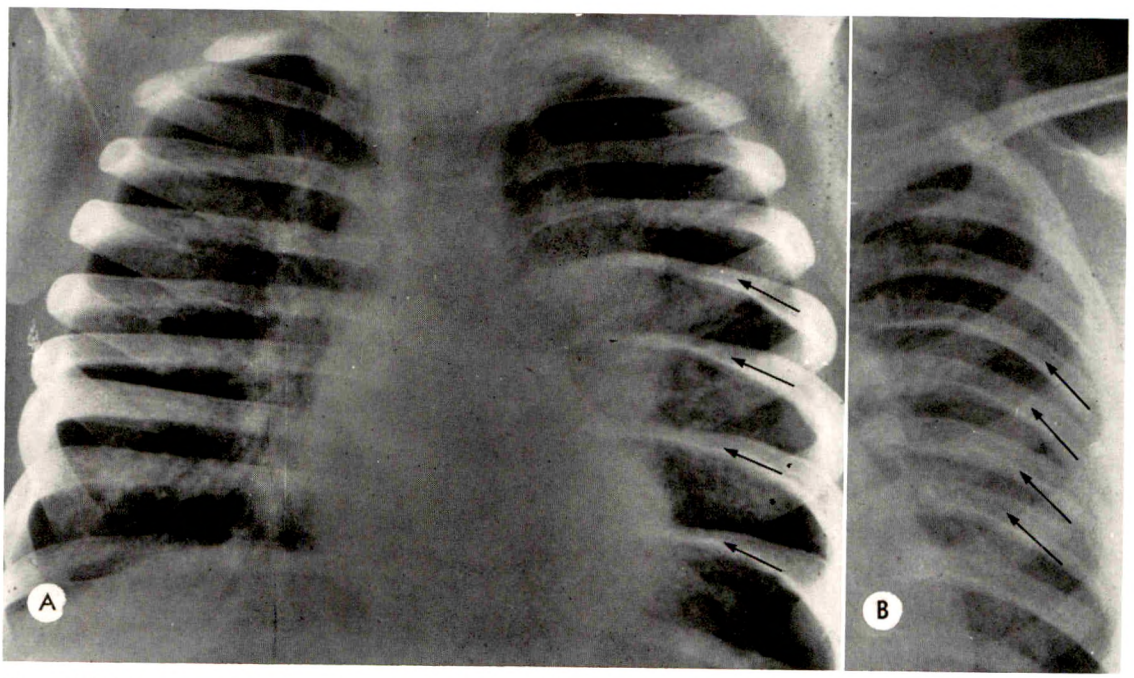


Fig. 9.* (*A*) A 1 year old infant with a thoracic neuroblastoma showing marked superior and inferior marginal rib defects involving the posterior aspect of the fifth through the eighth ribs on the left. (*B*) Complete restoration of the normal contour of the ribs following radiation therapy.

* From the Department of Radiology, University of Minnesota.

brae are often attenuated and show a twisted ribbon appearance.[14] Although such defects have been ascribed to pressure from adjacent intercostal neurofibromas,[19] some patients exhibiting this change do not have intercostal neurofibromas. Hunt and Pugh[15] state that although neurofibromas may contribute to skeletal deformities by pressure erosion, their inconstant presence and their limited distribution compared to the extent of the vertebral body deformities may minimize this consideration as the basic etiologic agent. Many of these patients have associated muscle weakness and this as well as a mesodermal or osteoid dysplasia may also be a contributing factor.

Although localized mechanical pressure and tension changes applied at right angles to the long axis of a cylindrical bone such as a rib result in resorption in the path of stress, the mechanism is not entirely clear.[1,23,34] There is decreased osteoblastic activity immediately subjacent to an area of excessive pressure, but there is also increased new bone formation at right angles to the point of pressure at some distance away. In the cases of multiple hereditary exostoses and in neurofibromatosis, osteodysplasias and muscle weakness may play a more prominent role than localized pressure in the formation of rib defects and deformities.

4. OSTEOGENESIS IMPERFECTA

Osteogenesis imperfecta is a systemic inability to produce adequate and normal osteoid in sufficient amounts to balance physiologic concomitant osteolysis. Although some primitive fiberbone is laid down, there is a poor transition to adult bone with poor lamellation and haversian system formation.[1] The bone cortex is deficient and lacks continuity. The bone that is formed remains in a coarsely fibered state, never becoming properly arranged according to the normal lines of stress.

Figure 10 illustrates generalized superior marginal rib thinning which is not due to any localized erosions. As a result of loss of normal bone rigidity, the ribs are rotated and curved abnormally. There is a concave superior margin seen in several ribs, which accentuates the fact that in many areas the superior cortical margins are thinned or absent.

5. MARFAN'S SYNDROME

Superior and inferior marginal rib defects in a patient with Marfan's syndrome are illustrated in Figure 11, *A* and *B*. A marked superior marginal defect is noted involving the left fifth rib. There is also bilateral notching of the inferior margins of several other ribs.

Leak[18] described a patient with thoracic cage deformity and rib notching involving both the superior and inferior rib margins. Clinical examination excluded coarctation of the aorta and indicated Marfan's syndrome with diffuse dilatation of the thoracic aorta and aortic incompetence with an increased pulse pressure. McCord and Bavendam[22] have suggested that an increased pulse pressure in the intercostal arteries can account for inferior rib erosions. However, this was rejected by Leak and, in addition, it could not explain the superior marginal rib defects. Rubin[27] has suggested that in the long slender tubular bones, the thinness of the diaphyseal cortex and shaft in Marfan's syndrome is probably due to poor muscle tone rather than to a primary alteration in the quality of osteoid bone formation. Hypotonic muscles, tendons and ligaments, a funnel thorax and pectus excavatum could all

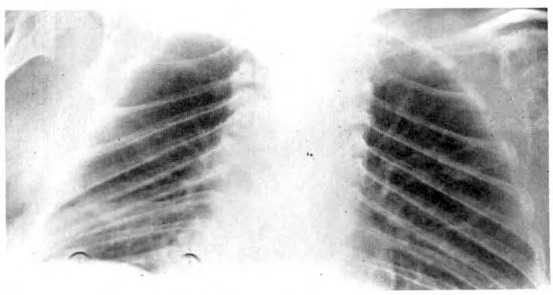


FIG. 10. A 28 year old male with a diagnosis of osteogenesis imperfecta. There are multiple curvatures of the ribs associated with loss of normal bone rigidity. There is a concave outline to the superior borders of the upper ribs often associated with thinning of the superior cortical margins.

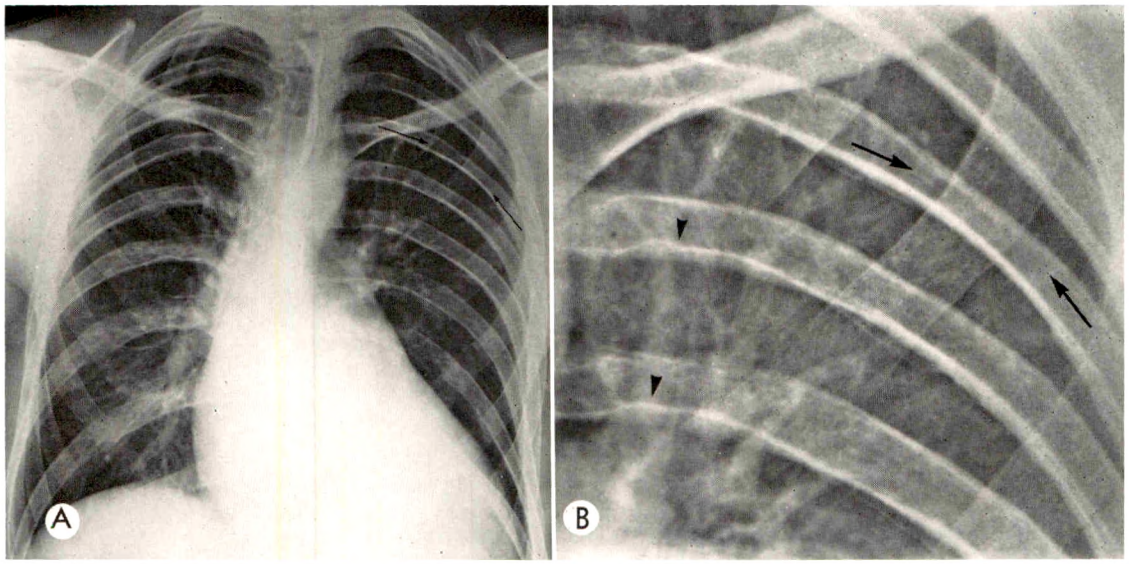


Fig. 11. (*A*) A 31 year old male with known Marfan's syndrome diagnosed at 6 years of age. At postmortem examination, aortic insufficiency associated with aneurysmal dilatation of the proximal aorta and aortic ring was found. No evidence of any abnormal arterial circulation was demonstrated in the region of the ribs. (*B*) Close-up view showing superior marginal defect of left fifth rib as well as inferior marginal defects of adjacent ribs.

result in loss of the normal muscle attachment stimulus to the cortical margins of a rib. This could explain localized marginal rib defects in patients with Marfan's syndrome who do not have related vascular anomalies.

6. RADIATION DAMAGE

The long term delayed effect of irradiation causing a localized superior marginal rib defect is illustrated in Figure 12, *A–D*. There is progressive superior marginal rib erosion over a period of 6 years in a patient who had a right radical mastectomy followed by extensive irradiation to the axillary and supraclavicular areas. No local or distant metastases could be demonstrated and the patient has actively used the right upper extremity since the surgical procedure.

The effects of localized irradiation on bone have been well documented.[27,32] Bone growth ceases and alterations in normal periosteal activity occur in a matter of days. Osteoclasts are less sensitive to damage than osteoblasts but both are probably affected and the normal balance between bone resorption and bone formation is affected. It is assumed in this case that the quantity of radiation was sufficient to interfere with normal osteoblastic activity. The occurrence of marginal rib defects many years following irradiation is a finding that should be looked for more frequently in patients who have had extensive irradiation to the thorax.

II. DISTURBANCE OF OSTEOCLASTIC ACTIVITY

1. HYPERPARATHYROIDISM

Noetzli and Steinbach[25] reported subperiosteal rib erosions in 6 of 16 patients with generalized hyperparathyroid bone disease. Characteristically, the defects occurred along the upper cortical margins of the posterior and posterolateral portions of the ribs and were more often unilateral. Boone *et al.*[8] described 1 case of hyperparathyroidism affecting the inferior rib surfaces and causing the appearance of true rib notching.

Figure 13, *A* and *B* illustrates marked superior marginal rib erosion involving the left sixth rib and a large "brown" tumor of the anterior end of the right fifth rib in a patient with severe hyperparathyroidism.

In hyperparathyroidism, parathormone

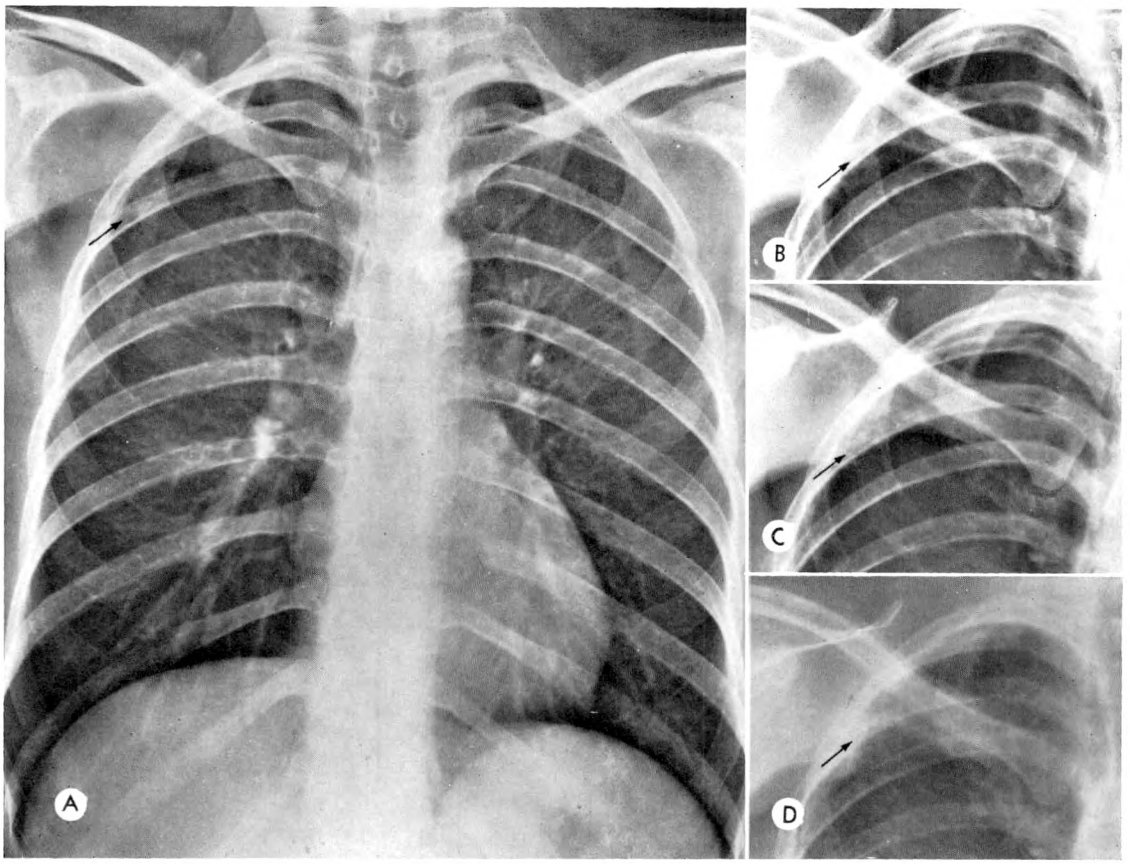


FIG. 12. (*A*) A 48 year old female who had extensive irradiation to the axillary and supraclavicular regions following a radical mastectomy for carcinoma of the right breast. Note original roentgenogram in 1962 with no evidence of superior marginal rib erosion. (*B*) Beginning thinning of the cortical margin of the fourth rib posteriorly at the superior aspect (1964). (*C*) Further progression of loss of outline of the superior margin of the fourth rib on the right (1965). (*D*) Complete loss of superior cortical margin of the fourth right posterior rib with preservation of the inferior cortical marginal outline. No evidence of localized or generalized metastatic disease was seen (1968).

has been shown to stimulate increased osteoclastic activity. Ascenzi and Marinozzi,[5] using a combination of modern modalities, microradiography, x-ray diffraction, polarizing microscopy and histochemical staining, concluded that the osteoclastic resorption is the only process responsible for the bone destruction found with parathyroid adenomas.

2. HYPERVITAMINOSIS D (?)

Figure 14, *A* and *B* is an example of superior marginal rib defects involving the left third and fourth ribs posteriorly, in a patient diagnosed by clinical and laboratory findings as vitamin D intoxication. A thyroidectomy had been performed 6 years previously, followed by hypoparathyroidism. The patient was treated with thyroid replacement, vitamin D and calcium lactate. She had been ingesting 100,000 units of vitamin D daily since the surgical procedure.

Parathormone,[5] vitamin D, [10, 37] and vitamin A[26] have the ability of destroying bone. Huge doses of vitamin D given to patients over a long period of time may precisely mimic the effects of parathormone.[1] Furthermore, damage to the kidney may result from hypervitaminosis D, leading to renal hyperparathyroidism and osteitis fibrosa cystica, thus further complicating the clinical and laboratory findings. Excessive osteoclastic activity with resul-

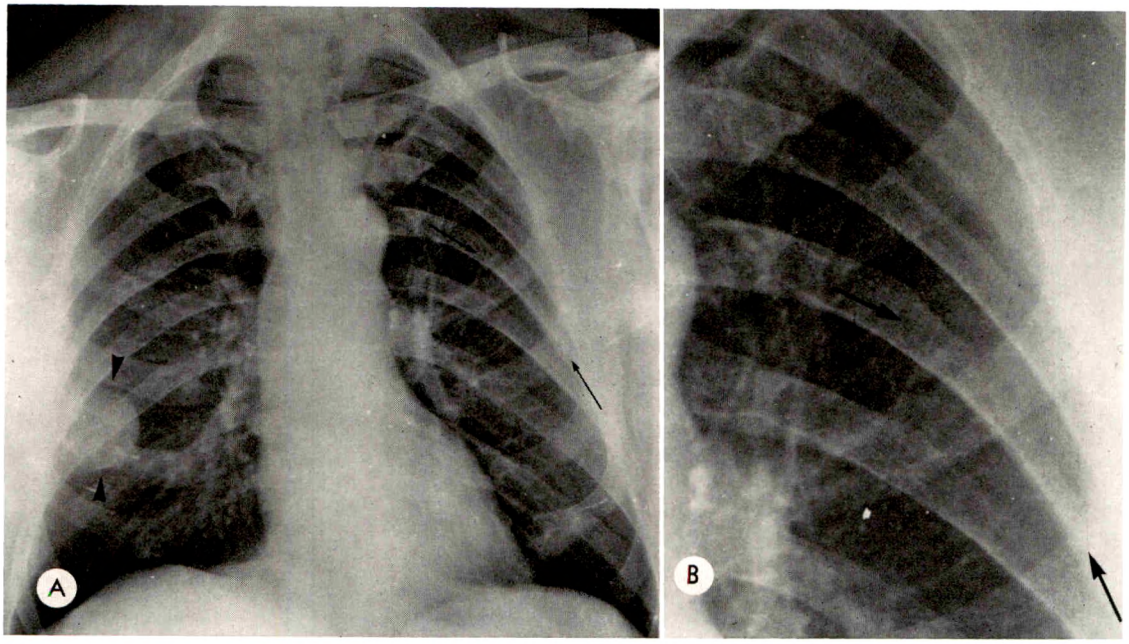


Fig. 13. (*A*) A 70 year old male with surgical removal of a parathyroid adenoma because of hyperparathyroidism. Biopsy of the mass at the level of the fifth rib anteriorly on the right showed a "brown" tumor. (*B*) Close-up view shows typical extensive superior marginal rib erosion of the left sixth rib.

tant subperiosteal bone absorption is probably the best explanation for the finding of rib defects in vitamin D intoxication. Although this finding has not been described in the very few cases of vitamin A intoxication, it is a theoretical possibility which should be kept in mind.

III. IDIOPATHIC RIB NOTCHING

Figure 15, *A* and *B* shows superior marginal rib defects involving the posterolateral portions of the fourth and fifth ribs on the right in a patient with idiopathic pulmonary fibrosis. Unequivocal superior marginal rib defects involving the fourth and

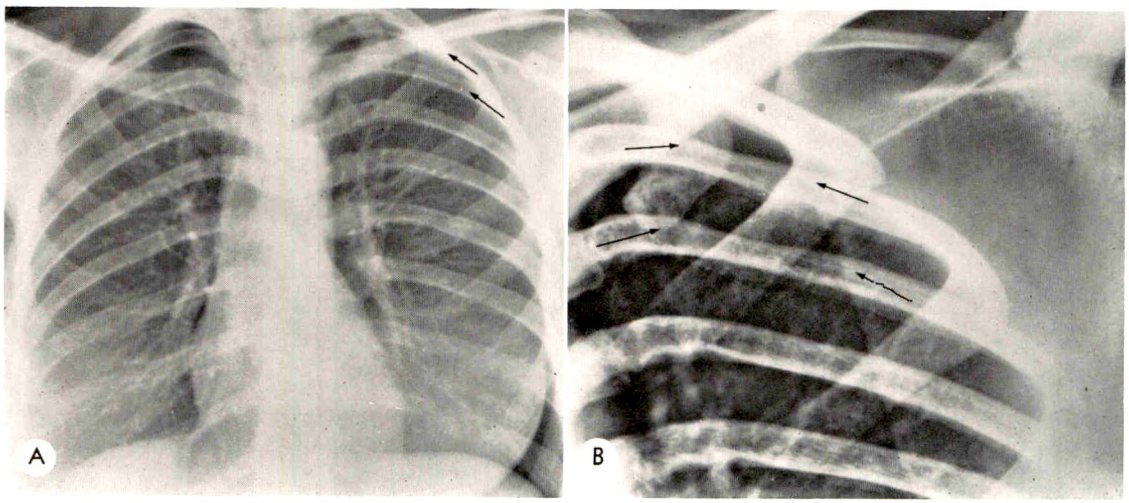


Fig. 14. (*A*) A 26 year old female with a thyroidectomy 6 years previously followed by treatment with thyroid replacement, vitamin D, and calcium lactate. Since that time she had been ingesting 100,000 units of vitamin D daily. (*B*) Close-up view shows typical superior marginal rib defect involving the left fourth rib, as well as a lesser degree of involvement of the left third rib.

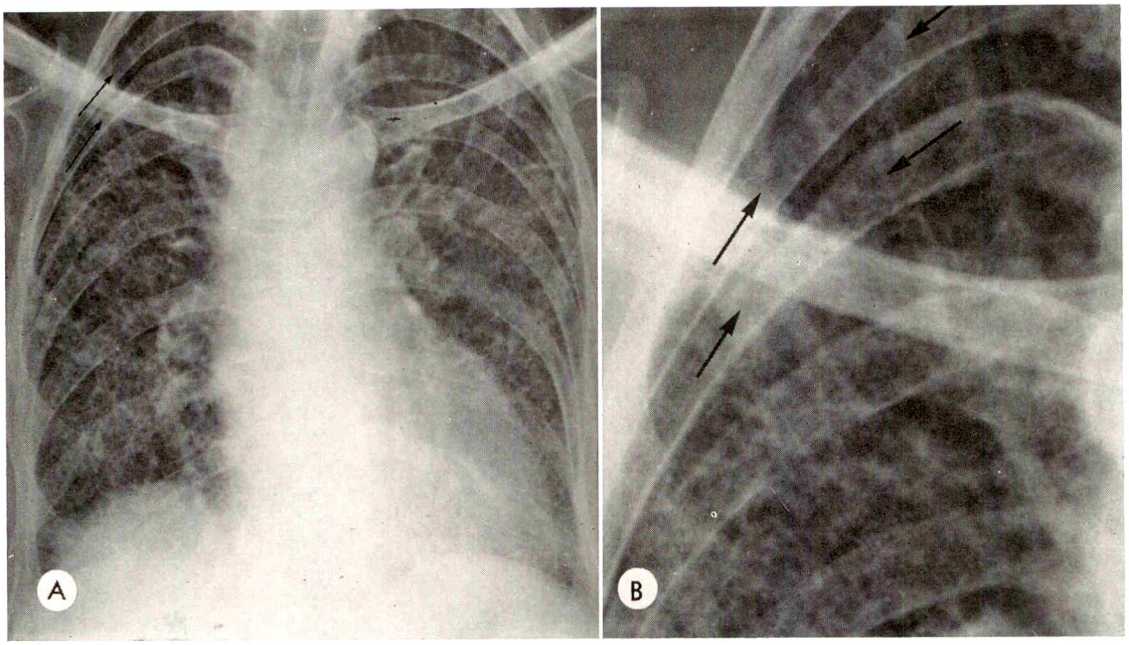


FIG. 15. (*A*) A 78 year old male who at postmortem examination showed cor pulmonale secondary to pulmonary fibrosis, presumably associated with the Hamman-Rich syndrome. (*B*) Close-up view showing loss of the superior margin of posterolateral portions of the right fourth and fifth ribs.

seventh ribs on the right and the fourth rib on the left were also recently found in a patient with chronic obstructive airway disease and pneumoconiosis. Thus there are occasional examples of unequivocal superior marginal rib defects in which a thorough investigation has failed to reveal any of the other causes mentioned. (Similar reports of idiopathic inferior rib notching have also appeared in the literature.[8,11,17])

DISCUSSION

Bone is a very plastic tissue, responsive to a great variety of stimuli in two basic ways—by new bone formation with osteoblastic activity and by destruction with osteoclastic activity. Genetic, hormonal, nutritional, mechanical, vascular, biochemical, and pathologic stimuli to bone formation and destruction—all in the final analysis—act by disturbing the cellular balance. How these factors act and why they manage to affect some cells in some bones in one way and other cells in different bones in another way, is not clear. It may also be that some parts of the same bone, particularly of a rib, are inherently more labile than others.

Based on retrospective and prospective studies, the causes of superior marginal rib defects were reviewed and classified. The list is relatively long and is probably not complete. Realizing that the classification presented may be somewhat artificial, nevertheless it is helpful in remembering the various disease entities that may be associated with superior marginal rib erosions.

Furthermore, one can predict with reasonable assurance that as one continues to search for this finding, additional causes will be encountered. With an arbitrary division into deficient osteoblastic activity in contradistinction to excessive osteoclastic activity, one is prompted to look for rib defects with hitherto unsuspected etiologies. When it was realized that excessive osteoclastic bone activity is found in vitamin D intoxication, the authors reviewed known cases and an unsuspected finding of superior marginal rib defects was discovered in 1 case. Similarly, since vitamin

A intoxication is also known to be associated with increased osteoclastic activity, a review of any known cases in adults might prove rewarding. If one were to investigate the numerous causes of neuromyopathies associated with thoracic musculature deficiencies, isolated cases of superior marginal rib erosions may also be uncovered. Other hormonal abnormalities resulting in osteoclastic-osteoblastic imbalance should also provide cases in which rib defects might also be encountered. Finally, any defective supply of raw material necessary for osteoid formation, *i.e.*, vitamin C and protein deficiencies (malnutrition, severe diabetes mellitus, hyperthyroidism, and nephrosis) might also provide additional case material for investigation of possible associated rib changes.

Not only is it easy to overlook minor degrees of superior rib erosion on the roentgenogram, but conversely one must guard against over-reading. In view of the frequency of minor and even moderate indentations of the ribs in normal individuals, it is sometimes difficult to be certain of pathologic defects. In this connection, measurement of the transverse diameter of a rib as compared to the adjacent ribs on the same and opposite sides of the thorax will be helpful.

In most cases, true superior rib erosion will show a decrease in thickness of the superior cortical marginal outline, but if this is preserved, the cortical margin must be unequivocally indented over a long area. Shallow elongated scalloping is just as reliable from the diagnostic standpoint as localized deeper, narrow solitary notches. Multiplicity of rib involvement strongly favors bona fide notching.

Kyphosis and lordosis, scoliosis and unusual positioning of the tube in relation to the patient can cause rotation of the posterior parts of the ribs on their longitudinal axis, causing pseudodefects simulating rib narrowing. Tuberous sclerosis can cause irregular cortical thickenings of ribs[9] simulating notched defects and this too should not be confused with true rib erosions.[8, 11, 36] These are possible pitfalls in diagnosis and are not to be confused with true rib erosions. Bucky films, tomograms, oblique views, and changes in positioning are helpful.

There are undoubtedly cases in which the rib defect or erosion is equivocal, and comparison with previous or subsequent roentgenograms will be helpful. Treatment of a localized etiology, such as removal of a neurofibroma or neuroblastoma following surgery, will often cause the rib to return to normalcy in outline. Removal of the cause of hyperparathyroidism will frequently cause the ribs to return to their normal configuration. With severe erosions and marked loss of bone substance, previous surgical procedures, metastatic malignancy, and even progressive osteolysis with disappearing bone[12] must be excluded in the differential diagnosis.

SUMMARY

Superior marginal rib defects are demonstrated in a variety of conditions. These are related for the most part to an imbalance between osteoblastic and osteoclastic activity.

The different mechanisms resulting in the bone defects are postulated and discussed. The many causes of superior marginal rib erosion are classified and examples are illustrated. Other disease entities in which superior marginal rib erosion might possibly be found are postulated so that the finding may be looked for and documented when encountered.

The finding is encountered with sufficient frequency that its diagnostic implications are important. Although nonspecific, the recognition of this sign on a chest roentgenogram should lead the roentgenologist to direct a further generalized investigation of the patient, resulting in a more definitive diagnosis.

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THE MEASUREMENT OF PROGRESSION IN PROTRUSIO ACETABULI*

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PROTRUSIO acetabuli is a relatively common condition associated with degenerative arthritis of the hip. The extent of the protrusion varies from patient to patient and in some patients even has been known to progress.[3]

The purpose of this study is to devise a simple method of measuring the progression of protrusio acetabuli in each patient and to correlate this with any change in the clinical assessment of the affected hip or hips.

MATERIAL

The roentgenograms of 242 patients with a diagnosis of degenerative arthritis of the hip who were admitted to Addenbrooke's Hospital, Cambridge over a 10 year period ending January 1, 1968, were examined. In 27 of these 242 patients, anteroposterior roentgenograms of the pelvis revealed protrusio acetabuli. In all, 40 hips in these 27 patients were affected.

Serial roentgenograms over a minimum period of 1 year and a maximum period of 13 years were reviewed in retrospect. The pelvic roentgenograms of 20 patients with normal hips were reviewed as a control. Any roentgenograms in which there was a tilt of the pelvis, as assessed by inequality of the obturator foramina, were discarded.

METHOD

On a standard 17×14 inch anteroposterior roentgenogram of the normal pelvis and hips (Fig. 1, *A* and *B*), the outline of the dome of the acetabulum meets the line of Köhler[4] at X′X. This line begins on the pelvic border of the ilium and ends on the medial border of the body of the ischium, brushing the dome of the acetabulum on its way. If the outline of the acetabular dome passes medial to Köhler's line, as in the left hip in Figure 2, *A* and *B*, a protrusion exists and the line X′X representing the maximum distance between them may be constructed precisely.

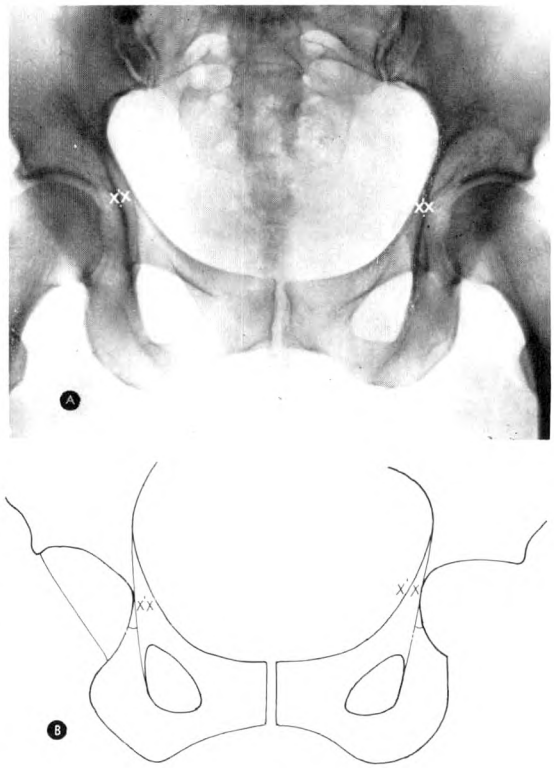


FIG. 1. (*A*) Anteroposterior roentgenogram of the pelvis and hip showing the normal position of Köhler's line. The outline of the dome of the acetabulum meets the line of Köhler at X′X. (*B*) Line drawing of *A*.

The protrusion distance X′X was measured by setting a ruler at right angles to Köhler's line; this gives a simple and direct measurement in millimeters. The distance X′X is called the protrusion distance.

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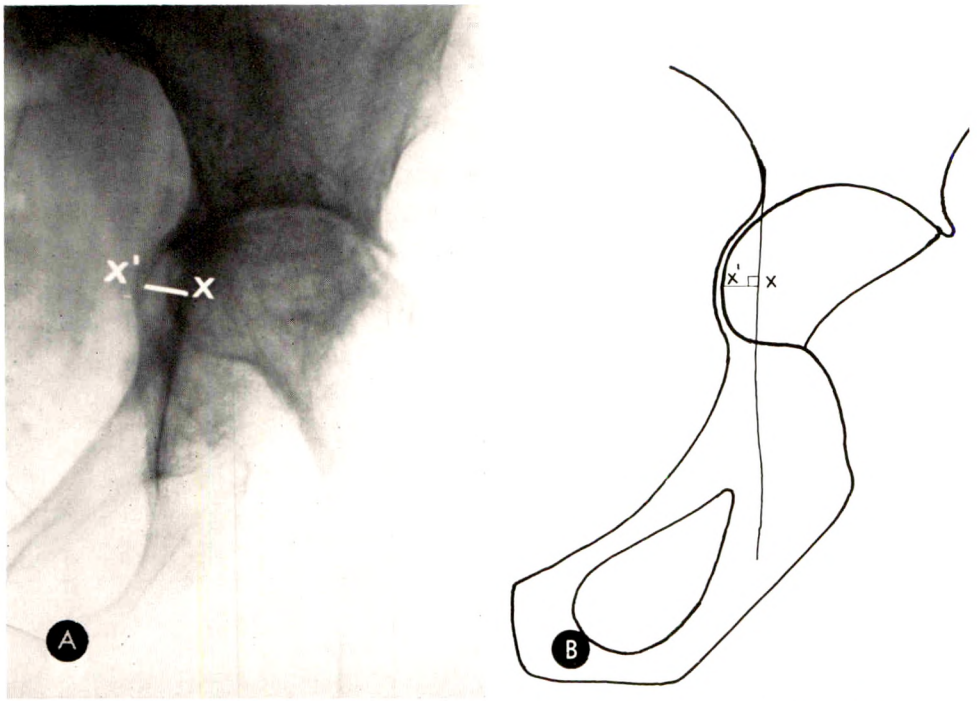


Fig. 2. (*A*) Roentgenogram of a left hip with protrusio acetabuli. The outline of the acetabular dome passes medial to Köhler's line. Therefore, a protrusion exists and the line X'X, representing the maximum distance between the line and the protrusion, can be constructed. (*B*) Line drawing of *A*.

Progression of this protrusion over the years can be measured (Fig. 3). For the first 2 years of observation in the patient shown in Figure 3, there was no protrusion; however, the roentgenogram at 4 years showed a protrusion of 5 mm. which progressed to 12 mm. at 7 years. In some normal hips there is a gap between Köhler's line and the acetabular rim lying more laterally. In these cases a negative protrusion distance may be said to exist.

RESULTS

The protrusion distance in the 40 normal hips was measured and was between 0 and −2 mm. In the patients with protrusion, 3 main groups emerged after measurement.

The first and largest group of 15 patients (20 hips) had progression of the protrusion by 2 mm. to 14 mm., with a mean of 6 mm. in a mean of 8.4 years.

The second group of 6 patients (10 hips) had no progression of the protrusion in a time ranging from 1 to 10 years, while the third group of 6 patients (10 hips) showed a small decrease in the protrusion distance, in fact, a regression.

All the hips with protrusion were assessed clinically and in retrospect, using the 4 class grading system of Shepherd.[5] All hips in the first (progressive) group clinically deteriorated by a minimum of 2 classes, while the nonprogressive group remained clinically unchanged. In the third (regressive) group, there was clinical improvement by at least 1 class.

DISCUSSION

Protrusio acetabuli has been defined as a condition in which the head of the femur lies further in the pelvis than normal.[2] The diagnosis of early cases is not usually accepted unless the "tear-drop" lines are crossed in a well centered film.[1] Quantitative assessment of the protrusion using the bitrochanteric diameter[2] is subject to error due to changes in the trochanter, neck and head of the femur, especially after arthro-

YEAR	PROTRUSION DISTANCE	
0	0 mm.	X' X
2	0 mm.	X' X
4	5 mm.	X'_4 X
7	12 mm.	X'_7 X

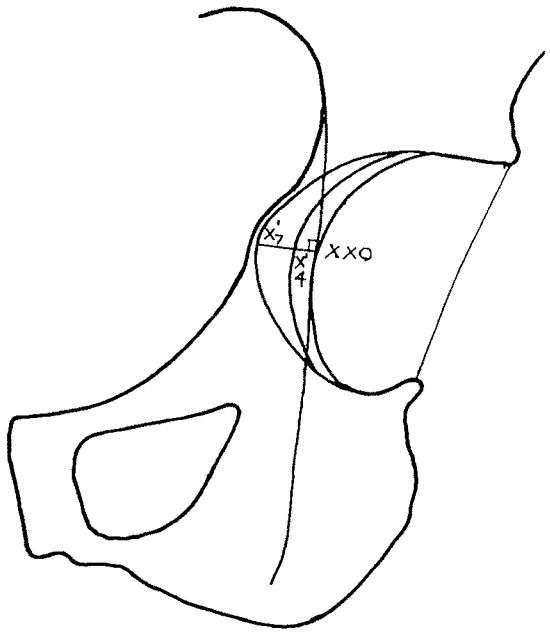


FIG. 3. Measurement of progression over the years in protrusio acetabuli.

plasty. If serial measurements are not made, and reliance is placed on clinical impressions of roentgenograms, early progression of a protrusion, with its serious prognostic significance, will be missed.

It must be stressed that this method is applicable to serial roentgenograms of individual patients and is not suitable for comparing 1 patient with another. Comparative measurements between patients have little value with regard to the management of each individual patient. A patient with a large protrusion is not necessarily more disabled than a patient with a small protrusion. It may be said that roentgen signs of degenerative arthritis in a hip with protrusion are of more value, but progression is often a very early sign, *i.e.*, before the gross changes of reduction in joint space or sclerosis have developed. The results of this study suggest that serial measurements will aid in identifying the slowly progressing cases of protrusio acetabuli who would benefit from early operation.

ERRORS

The standard error for the normal sample was 0.6, and for the protrusion sample, 0.65. The standard deviation from a mean of −0.4 was 0.7 for the normal sample and from a mean of +6, 3.4 for the protrusion sample.

SUMMARY

A method of measurement of protrusio acetabuli and its application are described.

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ROENTGENOLOGIC MANIFESTATIONS OF OSTEONECROSIS*

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ASEPTIC osteonecrosis without apparent relationship to trauma is not rare and, inasmuch as the radiologist may be the first to suspect the correct diagnosis, an awareness of the variety of roentgenologic manifestations which may be encountered is essential. This report is based on roentgenologic and clinical observations in 33 cases of this condition.

METHOD

The medical records and roentgenograms of all patients in whom the roentgenologic diagnosis of nontraumatic aseptic osteonecrosis was entertained during the past 5 years were reviewed. Thirty-three cases of this group were selected for inclusion in this study. Children with coxa plana (Legg-Calvé-Perthes' disease) were excluded.

The diagnosis was confirmed histologically in 16 cases. In 4 other patients the roentgenologic, clinical and surgical findings were considered diagnostic, but the material removed at operation (vitallium cup arthroplasty) was insufficient to permit an unequivocal pathologic diagnosis. Thirteen patients had not received surgical treatment. The earliest roentgenologic findings were non-specific in 7 of these, but repeated roentgenologic examinations over intervals ranging from 3 months to 8 years ultimately showed a characteristic appearance. In the 6 other patients there were typical roentgenologic and clinical findings from the outset. It should be emphasized that several cases were not included in this study because neither follow-up roentgenologic examinations nor pathologic proof could be obtained and the roentgenologic findings were not sufficiently characteristic to warrant a definite diagnosis.

RESULTS

SYMPTOMS

The pain associated with joint involvement was characteristically insidious but progressive. In only 2 instances had patients related a precise time of onset. It is noteworthy that some individuals who were not receiving steroid therapy had roentgenologic evidence of advanced bone necrosis with relatively little joint discomfort. However, some limitation of joint motion was usually present, particularly in severely affected cases.

DISTRIBUTION

The sites of involvement are shown in Table 1. In many patients a limited number of joints were examined roentgenologically and the possibility of relatively asymptomatic involvement of other joints could not be excluded. Hip involvement was observed in 32 cases and was bilateral in 24. Bilaterality was evident on the *initial* roentgenologic examination in all but 3 cases. In 3 other patients with asymmetric hip involvement at onset, the lesion was minimal on one side but progressed in 6 months, 2 years and 4 years, respectively.

TABLE I

DISTRIBUTION OF OSTEONECROSIS

Sites	No. of Patients		
	Unilateral	Bilateral	Total
Hip	8	24	32
Shoulder	0	2	2
Knee	0	2	2
Ankle	0	1	1
Wrist	1	0	1
Metadiaphyseal	0	2	2

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In 2 of these cases systemic steroid therapy was administered continuously during the interval. The hip disease remained unilateral in 8 cases and follow-up roentgenograms failed to show contralateral involvement after 3 years in 1 case and after 2 years in 2 other cases. Two patients with hip lesions exhibited bilateral necrosis of the humeral heads and 1 with systemic lupus erythematosus had lesions in both tali. One of 2 patients who had systemic lupus and necrosis of the distal femoral condyles had no other sites of involvement. An alcoholic patient who had bilateral hip lesions also had a sclerotic, compressed lunate. Two patients had calcified metadiaphyseal lesions in the long bones of the lower extremities in addition to joint involvement.

ASSOCIATED DISEASES AND STEROID THERAPY

The various diseases encountered in these 33 patients and the observations regarding prior steroid therapy are summarized in Table II. There were 6 cases of systemic lupus erythematosus and all had prolonged steroid therapy, with a minimum of 2 years of continuous treatment. One patient also had repeated injections into both knees and subsequently developed bilateral necrosis of the femoral condyles without hip involvement. Two patients with ankylosing spondylitis received steroid therapy for 5 and 9 years, respectively, a third patient with iritis was given steroid eye drops continuously for 6 month and 1 year intervals. Three patients with dermatitis received systemic steroid therapy in varying doses over 5 day intervals within a year of the development of osteonecrosis. Five patients were alcoholics and 2 of these had clinical and laboratory evidence of cirrhosis; various liver function tests in the other 3 patients were normal. One of those with cirrhosis had received both systemic and intra-articular steroid therapy because of a painful hip. Two of the 5 alcoholic patients had gout and neither had received steroids. Three additional patients with gout did receive systemic steroid therapy and 2 had intra-articular treatment as well. There were no patients with gout who did not have a history of either alcoholism or steroid therapy. Eight patients had miscellaneous conditions (Table II). The patient with ulcerative colitis also had asthma and all had received steroids except the hemophiliac. Five patients with bilateral hip involvement had no known disease, but 3 had received systemic steroid therapy elsewhere for unknown reasons.

A total of 24 patients received systemic steroid therapy and the type of drug varied

TABLE II

ASSOCIATED DISEASES AND PRIOR STEROID THERAPY

Disease	No. of Cases	Type of Steroid Therapy				
		None	Systemic		Intra-articular	Other
			>3 Months	<2 Weeks		
Lupus erythematosus	6		6		1	
Ankylosing spondylitis	3		2			1
Dermatitis	3			3		
"Alcoholism"	3	2	1		1	
"Alcoholism" and gout	2	2				
Gout	3		2	1	2	
Miscellaneous*	8	1	7			
None diagnosed	5	2	1	1	1	

* Rheumatoid arthritis, pemphigus, dermatomyositis, asthma, post renal transplantation, reticulum cell sarcoma, hemophilia, ulcerative colitis.

among virtually all presently available synthetic compounds. The daily dose ranged from maintenance equivalent dosages to high suppressive levels. The duration of treatment was greater than 3 months in 19 cases and less than 2 weeks in 5 cases. The therapy was administered prior to symptoms of osteonecrosis in all but 1 case. The latter was a patient with systemic lupus erythematosus in whom hip symptoms began prior to steroid therapy but roentgenograms were obtained afterward. Three of the 5 patients who received intra-articular steroids subsequently exhibited aseptic necrosis in the treated joints. However, all 5 patients received systemic steroid therapy as well and roentgenograms had not been obtained prior to the intra-articular treatment.

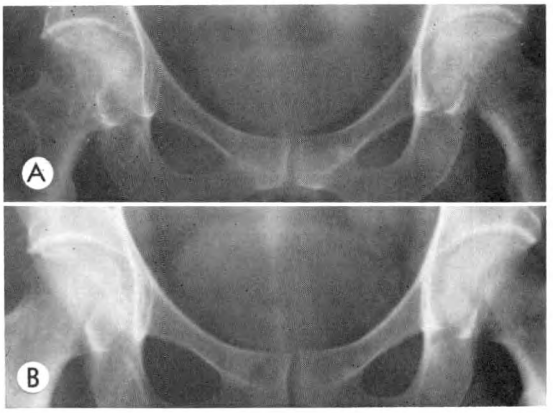


FIG. 1. (*A*) Diffuse mottling of both femoral heads due to osteonecrosis in a 43 year old Negro female with lupus erythematosus treated with systemic steroids for 3 years. Note the indistinctness of the subchondral cortices, particularly on the right, and minimal bone apposition at the femoral necks inferiorly. The cartilage spaces are relatively preserved. Compare with (*B*) showing normal hips in this patient 6 years earlier.

ROENTGENOLOGIC FINDINGS

The roentgenologic manifestations are summarized in Table III. A diffuse mottling of the femoral heads with apparent erasure of the trabecular pattern was noted in 11 cases (Fig. 1, *A* and *B*; and 2, *A* and *B*). In 16 patients there were discrete, irregular lucencies with surrounding sclerosis (Fig. 3; and 4*A*). In 7 cases there was a patch of increased density, often ill-defined and adjacent to small areas of rarefaction (Fig. 5*B*; and 8). Occasionally this was the earliest finding. The "rim sign," consisting of a subchondral bone fragment, slightly separated from the rest of the bone, was noted in 16 cases (Fig. 4*B*). When seen in the femoral or humeral head it was often crescentic but a comparable fragment which paralleled the subchondral plate was observed in the talus (Fig. 6, *A-D*). Laminagrams were occasionally helpful (Fig. 5*D*). A more generalized fragmentation of the subchondral bone was present in 8 instances (Fig. 7). Varying degrees of depression of the subchondral cortex were noted in 26 cases (Fig. 3; and 5, *A* and *C*). A large defect in the end of the bone, giving an appearance as though a bite had been taken out of it ("bite sign"), (Fig. 2, *C* and *D*; 8; and 9, *A* and *B*) was an outstanding feature in 4 cases. Periosteal bone apposition of the femoral neck, usually involving the inferior aspect, was demonstrated in 24 cases (Fig. 1*A*; 7; and 8). In 1 of these cases a microfracture with callus formation was evident histologically at the inferior aspect of the junction of the femoral head and neck. There were 2 patients, both with femoral head involvement, who exhibited changes suggesting bilateral necrosis of the femoral trochanters. In 1 patient with systemic lupus erythematosus the femoral trochanters

TABLE III

ROENTGENOLOGIC FEATURES OF OSTEONECROSIS

	No. of Cases
Mottled trabecular pattern	11
Localized rarefactions, some sclerosis	16
Patchy sclerosis, some rarefactions	7
"Rim sign"	16
Generalized subchondral fragmentation	8
Subchondral depression	26
"Bite sign"	4
Periosteal bone apposition	24
Acetabular protrusion	5
"Degenerative changes"	5

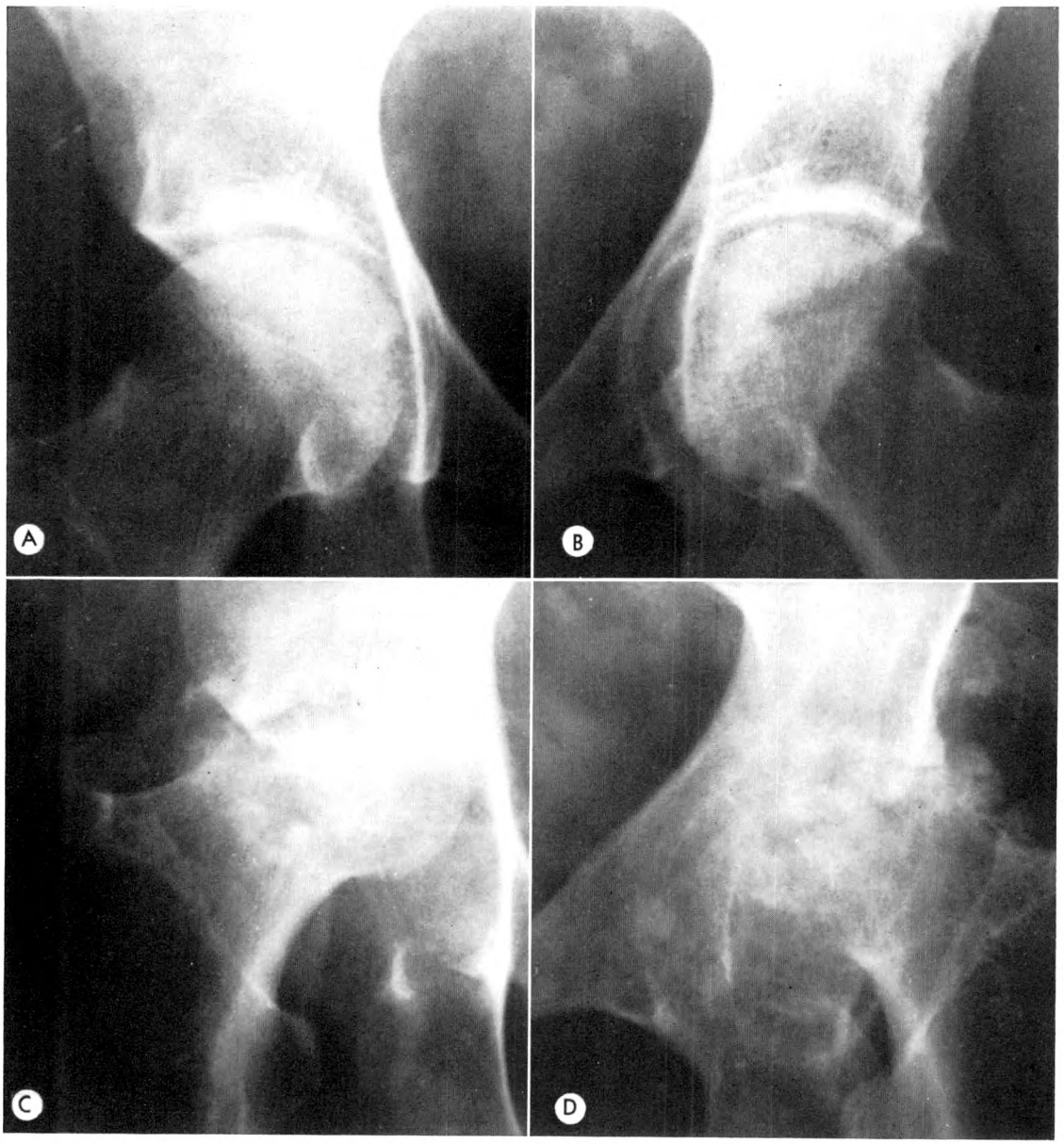


FIG. 2. (*A* and *B*) Right and left hips in a 40 year old white female with lupus erythematosus who had received steroids for many years. There is bilateral osteonecrosis, particularly on the left, indicated by diffuse mottling of the trabecular pattern in the head. Note the focal areas of new bone formation at the superior aspects of the femoral neck (particularly on the right), presumably due to stress fractures, and the slight acetabular protrusion, particularly on the left. (*C* and *D*) Right and left hips, 6 years later. Advanced fragmentation, compression and resorption of necrotic bone, the so-called "bite sign." The lesion in the right hip was verified histologically.

were sclerotic (Fig. 10, *A* and *B*) and in another, in whom there was no associated disease or prior steroid therapy, there were mottled rarefactions in these areas (Fig. 11). Inward protrusion of the acetabular margins accompanied involvement of the femoral head in 5 patients but in none was this severe (Fig. 2*B*) and all 5 had moderate osteoporosis. Cartilage space narrowing and hypertrophic spur

formation in the hips were late manifestations in 5 cases, resulting in an appearance which could be confused with degenerative joint disease (Fig. 12, *A* and *B*).

DISCUSSION

Osteonecrosis has been implicated as a complication of a number of systemic conditions[16] including sickle cell disease, decompression sickness, Gaucher's disease, alcoholism, pancreatitis, gout, lupus erythematosus and hypercortisonism. However, in some of these conditions the nature of the relationship, and, indeed, whether there is a relationship at all, remains to be determined. The theories of pathogenesis that have been proposed often fail to clarify the precise mechanism involved and leave a good deal unexplained. In sickle cell disease, for example, bone necrosis presumably results from intravascular thromboses secondary to sickling of erythrocytes. Although this complication has been observed in patients with homozygous sickle cell hemoglobin,[41] where crises are frequent and severe, it is at least as common, if not more so, in sickle cell-hemoglobin C disease and sickle cell-thalassemia,[28,35] where sickling occurs *in vivo* only under extreme conditions of anoxia. In considering this apparent paradox, Rucknagel and Neel[35] have suggested that higher hematocrits attained in the sickle cell variants may permit a slower capillary circulation than occurs in homozygous sickle cell anemia, allowing time for intravascular sickling. Osteonecrosis has recently been reported in cases of hetero-

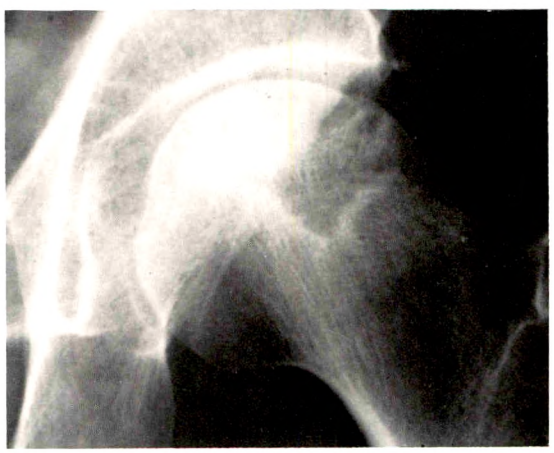


Fig. 3. There is an irregular, circumscribed rarefaction in the subchondral bone, bounded by a fuzzy zone of sclerosis, which proved to be aseptic osteonecrosis. The patient was a 52 year old white male who had no known disease but had been treated with systemic steroids for "joint complaints." Note the slight depression of the subchondral cortex beneath the outer margin of the acetabulum and the preservation of the cartilage space.

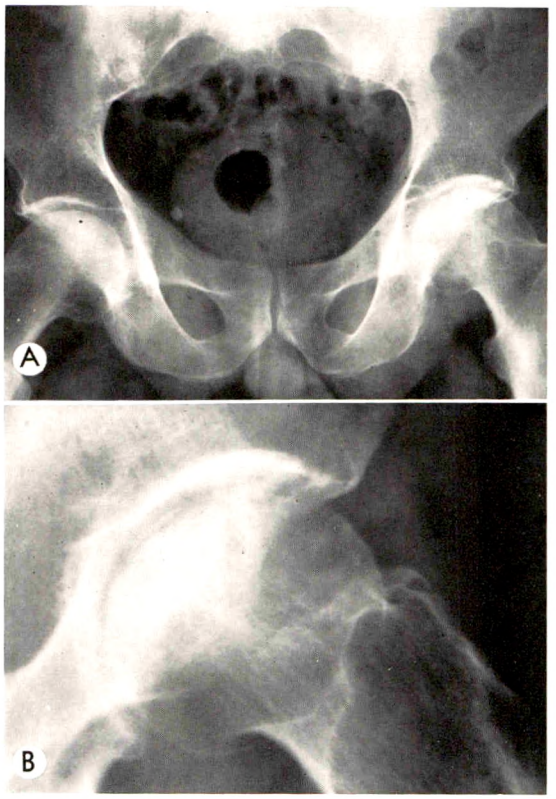


Fig. 4. (*A*) Aseptic necrosis of the left hip in a 52 year old male with ankylosing spondylitis who received systemic steroids for 9 years. There is a subchondral zone of rarefaction bounded by an indistinct area of sclerosis in the femoral head and a similar smaller area is present at the junction of the head and neck. The subchondral cortex is indistinct but the cartilage space is relatively preserved. (*B*) The lateral roentgenogram of the left hip, obtained at the same time, shows the extent of the subchondral necrotic zone, situated anteriorly, and clearly delineates the "rim sign." The diagnosis was verified pathologically.

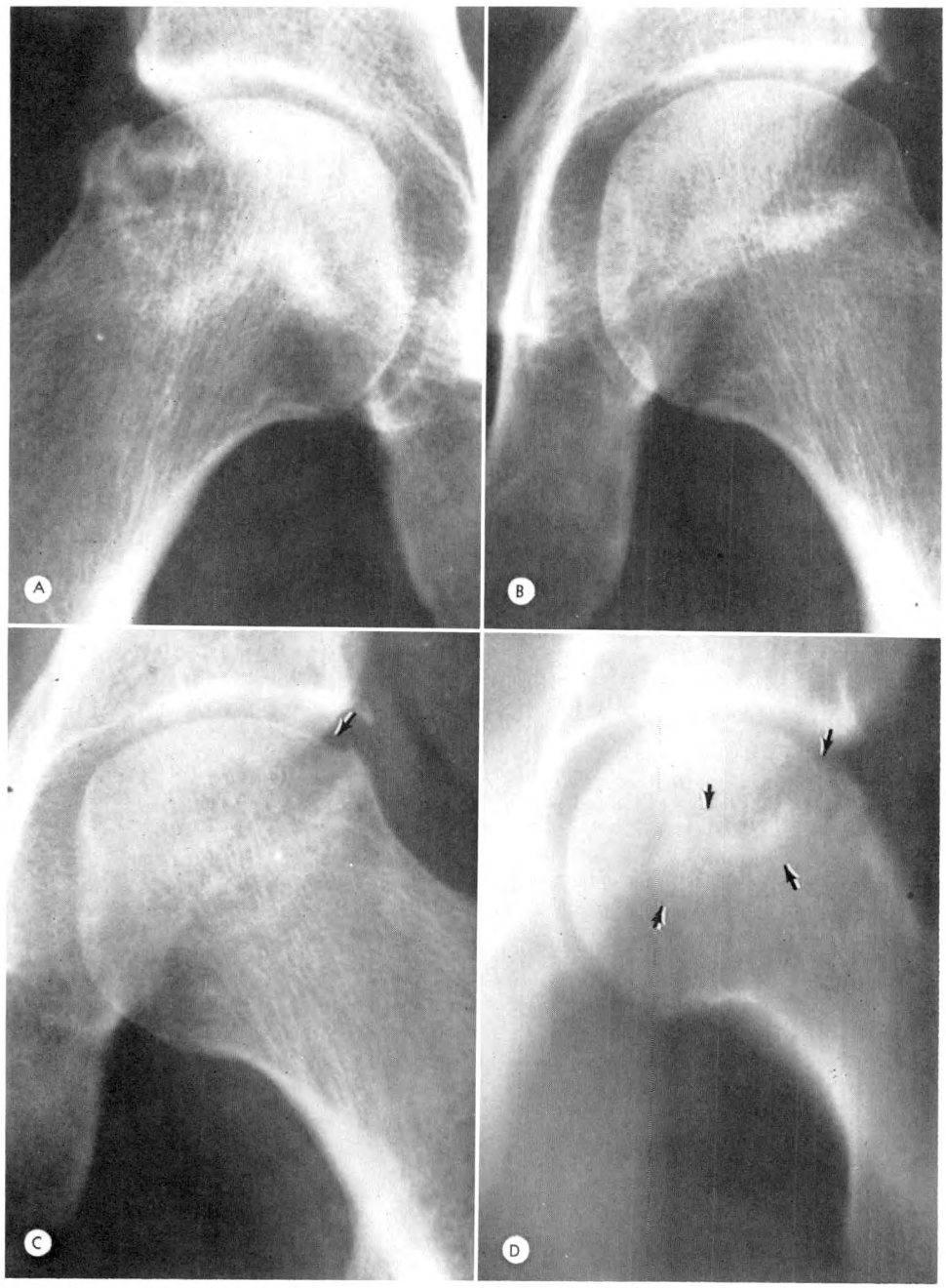


FIG. 5. (*A*) A 37 year old white male with gout who had been treated with steroids manifested an irregular rarefaction with adjacent sclerosis and focal depression of the subchondral cortex in the right hip. The lesion was verified pathologically as osteonecrosis. (*B*) At this time there was only an irregular patch of sclerosis in the left hip. (*C*) Six months later there was a slight depression of the subchondral cortex of the left hip (arrow) and a suggestion of a faint, indistinct zone of rarefaction medial to this. (*D*) A laminagram at this time showed a small fracture line (top arrow) adjacent to the irregular zone of sclerosis (arrows). Extensive osteonecrosis of the left femoral head was subsequently verified histologically.

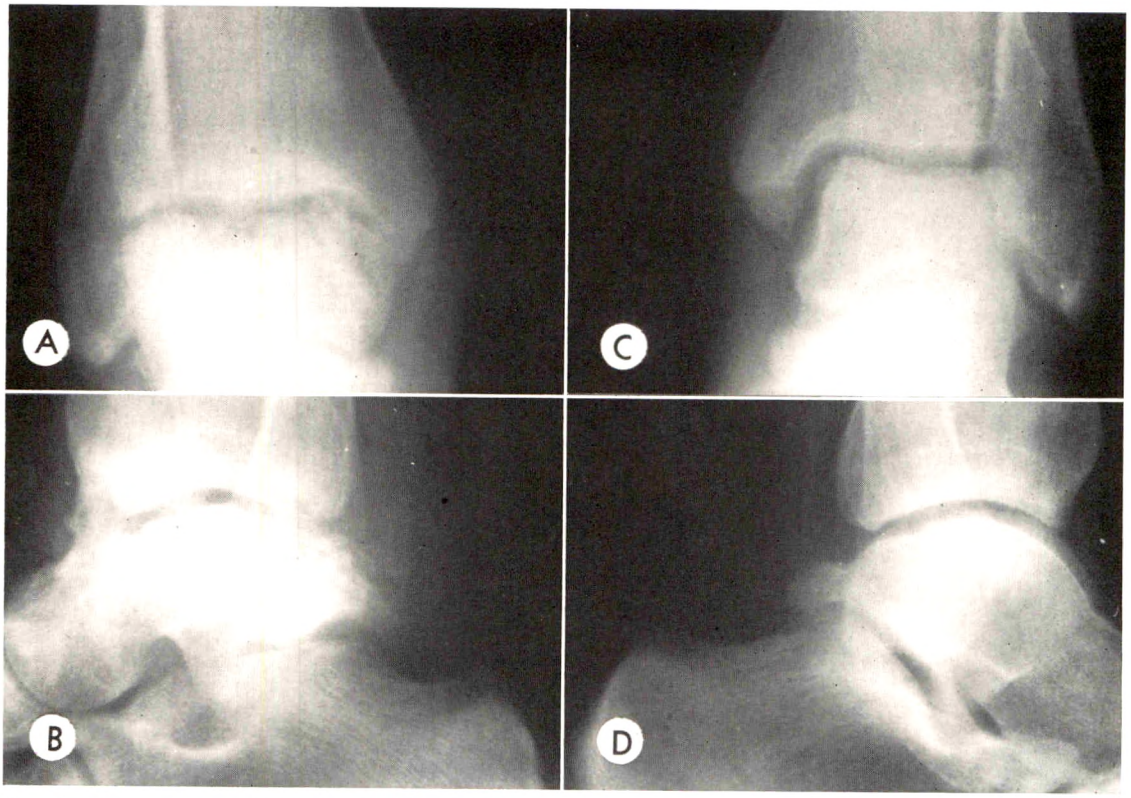


Fig. 6. Bilateral necrosis of the talus in a white female with lupus erythematosus, aged 20 years, who received systemic steroids for 3 years. (*A* and *B*) Note the extensive subchondral involvement with compression on the right and (*C* and *D*) the minimal lesion on the left with a suggestion of a fracture line paralleling the slightly depressed, subchondral cortex of the talus. The hips and shoulders were also involved (see Fig. 10).

zygous sickle cell trait[1] but, inasmuch as the latter is common in Negroes and the former is relatively rare, this relationship may be questioned. However, the possibility of an association warrants that electrophoretic hemoglobin analyses be routinely included in the evaluation of all Negro patients with osteonecrosis.

Gout and hyperuricemia have been suggested as causes of osteonecrosis and uric acid crystals have been found in the synovium of osteonecrotic joints in these conditions.[13,26] The deposition of urate, however, may be a secondary phenomenon. Urate deposits were unsuccessfully sought for in the resected, necrotic femoral head of one of our gout patients who had been treated with steroids. As our experience has suggested (Table 11), other factors may be responsible for this complication in gout. Serre *et al.*[38] likewise observed 3 patients with aseptic necrosis among 150 cases of gout and all 3 had been treated with steroids; Rotés Querol and Munoz Gómez[34], in a study of hip involvement in 370 cases of gout, found no examples of avascular necrosis. A direct relationship of gout to osteonecrosis has yet to be proved.

Fat embolization associated with altered fat metabolism[22] has been postulated as the mechanism of bone infarction in chronic alcoholism,[18,19,32] and in pancreatitis a lipolytic action of circulating pancreatic enzymes has been suggested.[10] It may not be possible to ascribe significance to one or the other factor when these conditions coexist, as they often do. Both metadiaphyseal and epiphyseal lesions occur in both these conditions as well as in the



FIG. 7. Bilateral necrosis in a 47 year old male who was treated intermittently with relatively small doses of systemic steroids for exfoliative dermatitis. He also had a history of moderate consumption of alcohol. There is advanced fragmentation of the necrotic bone, secondary hypertrophic bone formation at the joint margins and narrowing of the cartilage spaces. Note the extensive bone apposition at the femoral necks as seen in osteoarthritis.

"bends." The metadiaphyseal lesions are thought to be due to intramedullary fat necrosis,[14] and whether the epiphyseal lesions are secondary to this or due to concurrent embolic occlusion is not clear. In Gaucher's disease vascular obstruction may occur secondary to osseous infiltration by Gaucher cells or there may be intraosseous embolism of these cells,[42] whereas in hemophilia the necrosis is presumably due to intraosseous hemorrhage.[28] It is conceivable that in both conditions, the weight-bearing bone collapses as a result of the primary pathologic process and secondary necrosis supervenes. Osteonecrosis may occur in systemic lupus erythematosus but corticosteroid therapy is so widespread in this condition that it may be difficult to know whether the disease or the treatment is responsible. This complication has apparently been observed prior to steroid therapy.[7,36,39]

An important phenomenon is the induction of osteonecrosis by steroid therapy.[6,12,33,40,43] Although much evidence has accumulated in support of this relationship, the underlying mechanism has not been elucidated nor has this phenomenon been duplicated in animals.[3] Increased blood coagulability, thromboembolism, vasculitis, a Charcot-like effect secondary to joint analgesia and osteoporosis with "fatigue osteoarthropathy" have been theorized.[3,9,16,17,25] Conclusive evidence of vasculitis as a cause has not been documented and it could be difficult to detect in the resected necrotic bone. It is possible that some patients with steroid-induced osteoporosis may develop compression fractures with small secondary foci of bone necrosis. However, this phenomenon would hardly explain all the lesions described here. The bones in many cases are of near normal density, and vertebral compression deformities characteristic of osteoporosis are often absent.[12] Furthermore, the theory of steroid-induced osteoporosis with secondary fatigue fractures fails to explain the



FIG. 8. Bilateral necrosis in a 43 year old male who was a chronic alcoholic for 20 years. There is a good deal of destruction of the subchondral bone, with fuzzy marginal sclerosis and periosteal bone apposition at the femoral necks. Note the isolated patch of sclerosis, suggesting an additional zone of necrosis, in the left femoral neck.



FIG. 9. (*A*) Bilateral necrosis in a 59 year old male with gout who had received steroids intermittently for 10 years. Large lytic areas with surrounding sclerosis occupy the entire femoral head bilaterally. Note the discrete fracture line (arrow) on the left. (*B*) Six months later. There is further compression and resorption of necrotic bone giving an appearance as though a bite had been taken out of the femoral head.

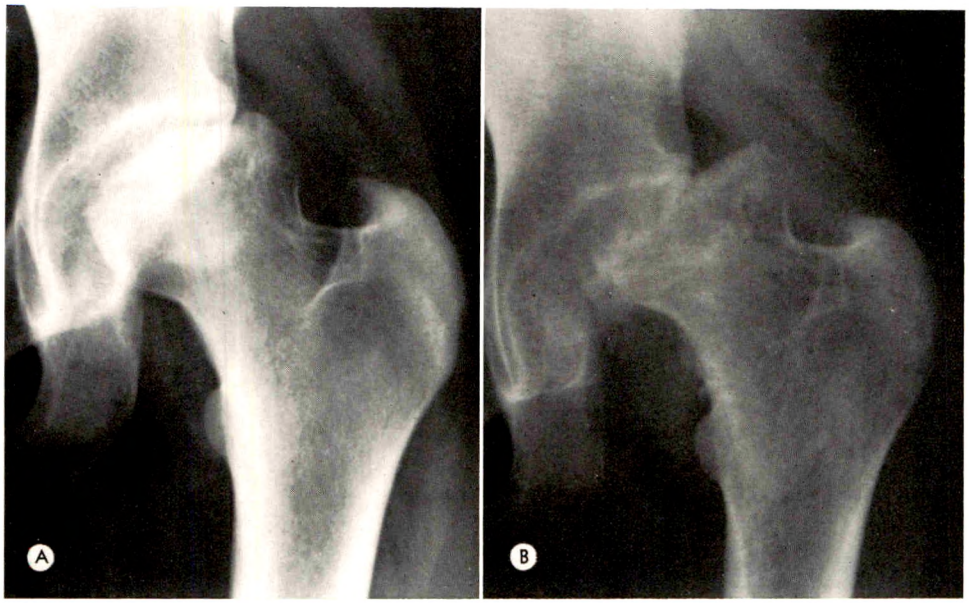


Fig. 10. (*A*) Same patient as in Figure 6. Advanced necrosis of the femoral head with sclerosis of the greater trochanter, probably also representing bone necrosis. (*B*) One year later. Further compression of the necrotic subchondral, weight-bearing bone but no change in the greater trochanteric region. Note bone apposition at the femoral neck. Osteonecrosis of the femoral head was verified histologically.

typical *subchondral* distribution of these lesions and the occasional involvement of non-weight bearing joints; fractures at these sites with subsequent extensive osteonecrosis are unusual in osteoporosis due to other causes. The small stress fractures which may be observed in the femoral neck adjacent to the necrotic head may be secondary to the altered mechanics within the joint following bone necrosis, inasmuch as bone formation in the femoral neck was not usually an early manifestation in these cases. It is of interest that there are relatively few reported cases of Cushing's syndrome with osteonecrosis as a complication.[23,32] Perhaps it is the *exogenous* steroid preparation which is responsible or possibly *fluctuation* in the level of circulating steroids is important. Symptoms of osteonecrosis often first develop after steroid withdrawal and this has been noted by others.[2] However, bone necrosis may be relatively asymptomatic and it is probably the late secondary effects on the joint or periosteum which are painful;[14] it is quite possible, too, that symptoms are masked by the steroids and the lesion becomes painful upon steroid withdrawal.

Johnson[14,15] theorized that in hypercortisonism increased deposition of marrow fat, possibly triggered by angiitis, may cause compression of the marrow sinusoids with necrosis of the bone marrow and, secondarily, of the bone. According to him, the seat of the pathology is in the bone marrow rather than the bone and he cites the distribution of necrosis in the femoral heads as precluding arterial and venous blockade explanations. To be sure, the bones most frequently affected, the femora and humeri, have a relatively high marrow content with small amounts of red marrow in the bone ends and a large quantity of fatty marrow in the diaphysis. However, although steroids induce fat deposition, they also stimulate red marrow and there is no evidence, to our knowledge, that there is an actual increase in fatty marrow at the ends of these bones in steroid-treated patients. Furthermore, calcified metadiaphyseal lesions representing intramedullary fat necrosis, are said to be uncommon in hypercortisonism.[16] It is possible that steroids,



FIG. 11. A 53 year old white female with idiopathic, histologically-confirmed necrosis of the femoral head. Note the mottled rarefaction and sclerosis in the greater trochanter, probably also representing osteonecrosis. There were similar lesions in the metadiaphyseal regions of the long bones.

particularly the synthetic compounds, induce a qualitative change in the marrow fat, which interferes with marrow circulation either grossly or via enzyme transport. Jones and co-workers[17,19] have recently suggested that fat embolism is the cause of osteonecrosis in hypercortisonism (as in alcoholism) and that the source of these emboli is the corticoid-induced fatty liver. The profound alteration in fat metabolism in patients receiving steroid therapy strongly points toward this as a factor in the causation of osteonecrosis and the theories advanced both by Johnson and Jones *et al.* are equally attractive. However, the evidence is largely circumstantial and speculative and direct experimental proof for any of these theories has yet to be brought forth.

Five patients received steroid therapy for less than 2 weeks. The role of such short term treatment in causing osteonecrosis is unclear. Possibly, short term treatment can be significant if the dosage is high enough. It is conceivable, however, that in these 5 cases the steroid therapy was unrelated and other factors were responsible, inasmuch as the dosages were not particularly high. Whether intra-articular steroid therapy causes osteonecrosis is likewise not clear.[21] All of our patients treated intra-articularly also received systemic therapy. Steroids are rapidly absorbed into the blood when injected into inflamed joints,[45] and a systemic effect may therefore be postulated. However, patients receiving systemic treatment may manifest insidious joint symptoms due to osteonecrosis and may then be treated with intra-articular injections for these symptoms. Recently, animal experiments have suggested that intra-articular steroids have a deleterious effect on the articular cartilage itself.[24,29,37] However, the relevance of this observation to clinical situations may be questioned in view of the short half-life of steroids within the joint[45] and the complete reversibility of *in vivo*, steroid-induced modifications of cellular function following hormone withdrawal.[4]

The roentgenologic manifestations of osteonecrosis are largely a consequence of fragmentation, compression and reabsorption of dead bone, on the one hand, and the proliferation of granulation tissue, revascularization and production of new bone on the other. In patients in whom there is a significant inhibition of osteogenesis, as in prolonged or intensive steroid therapy, fragmentation and extensive bone resorption, rather than bone production, may be expected. In such cases one can expect a rapid deterioration of the joint and an appearance which has prompted the term "Charcot's arthropathy."[5] The "bite sign" refers to extensive, sharply marginated subchondral bone resorption, as though a bite had been taken out of the bone, and this finding has recently been described as a manifestation of "steroid arthropathy."[27] Four of our patients exhibited this sign and, indeed, all 4 had received steroid therapy but the presence of osteonecrosis was verified histologically

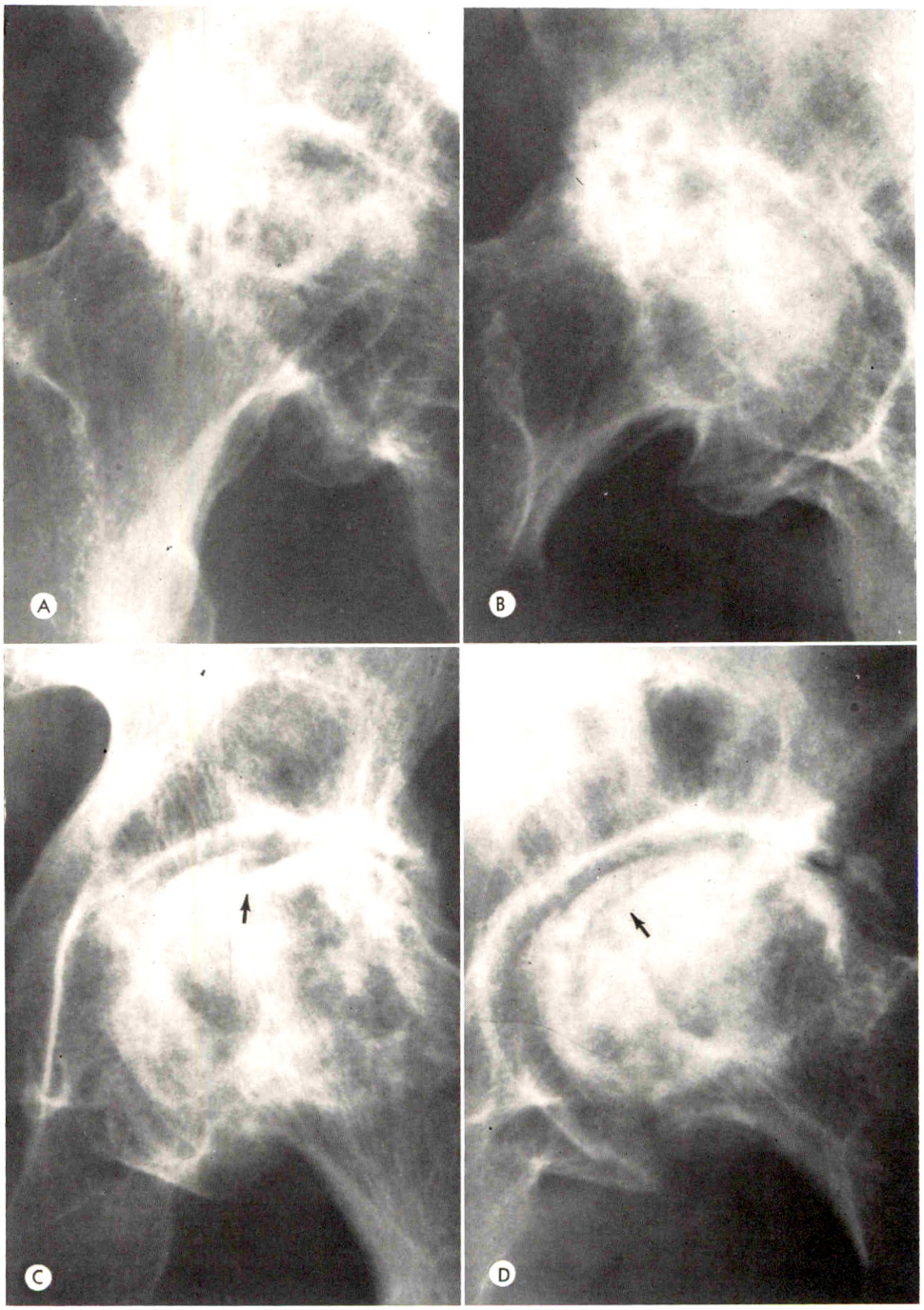


Fig. 12. (*A*) Anteroposterior view, right hip. Advanced necrosis of the femoral head with secondary hypertrophic degenerative changes in a 62 year old white male who first developed symptoms 2 months after systemic steroids were administered for dermatitis. (*B*) The lateral projection may be confused with osteoarthritis. (*C* and *D*) Anteroposterior and lateral projections of the left hip show a large irregular lytic area in the femoral head with fractures through the necrotic subchondral bone (arrows).

in 2 cases. One may speculate that such "steroid arthropathy" in some instances represents unrecognized osteonecrosis in which there is inhibition of reparative osteogenesis leading to rapid joint deterioration. Recent observations have suggested that lipids occur normally in both compact bone and spongiosa[8] and it is possible that certain specific lipids participate in an enzyme transport mechanism necessary in bone metabolism. Conceivably, steroids may affect the distribution of these lipids within bone, preventing normal mineralization. In addition they have a known catabolic effect which interferes with osteoid formation.

The osteonecrotic area within a joint almost always involves the subchondral zone. In the hip it is usually in the outer, anterior portion of the femoral head. The lateral or "frog" view is indispensable, particularly in detecting small lesions situated anteriorly. The characteristic, narrow, crescent-shaped line, first described by Waldenström[44] in 1938 and more recently by Norman and Bullough[31] may be visualized in the lateral projection only (Fig. 4, *A* and *B*). This line, which may also be observed in Legge-Calvé-Perthes' disease,[44] represents a fracture through the necrotic subchondral bone (Fig. 12, *C* and *D*). Slight depression of the subchondral cortex is a more common manifestation caused by compaction of the underlying necrotic bone. In neglected cases the latter may undergo extensive fragmentation and compression.

The lesion, as seen in the gross specimen, is often a wedge-shaped zone with the apex directed toward the center of the femoral head and the base adjacent to the articular cartilage. The roentgenologic counterpart is a discrete, irregular rarefaction bordered by a fuzzy, sclerotic zone (Fig. 3) and, although its configuration will depend on projection, it is rarely seen as "wedge shaped." A frequent and relatively early manifestation which is subtle and easily overlooked consists of a mottling of the trabecular pattern (Fig. 1*A*; and 2*B*). The earliest manifestation of bone necrosis, however, is probably "osteosclerosis." It may be confined to a small area and its significance may then be misinterpreted as a "bone island" (Fig. 8). In one patient with advanced necrosis of a hip, there was such a zone of increased density in the opposite femoral head and this progressed to obvious necrosis 6 months later (Fig. 5, *B*, *C* and *D*). Furthermore, in view of the frequency of bilateral involvement, there should be a high index of suspicion in such patients with osteonecrosis of a single joint.

Periosteal bone apposition is common in aseptic necrosis of the hip in adults. It occurs in the femoral neck, particularly at the inferior aspect and, although this has been noted previously,[11] its frequency and significance have not been emphasized. It occurs in osteoarthritis of the hip[30] where it probably represents a buttressing of the bone secondary to stress alterations which follow changes in weight-bearing at the femoral head. Its pathogenesis in osteonecrosis is probably similar, and the pathologic demonstration of a microfracture at the junction of the necrotic femoral head and neck in one of our patients who did not receive steroid therapy or have a history of trauma supports this view. In Legg-Calvé-Perthes' disease there is an analogous widening of the femoral neck as the head becomes flattened and deformed.

Involvement of the femoral trochanters, presumably by osteonecrosis, in 2 of our patients is noteworthy and has not to our knowledge been previously described. The observation of acetabular protrusion is also of interest. It was bilateral in all cases and may have been due to osteoporosis. Four of the 5 patients who exhibited it had received steroids. Abnormal stress directed medially at the acetabulum may also have been a factor.

The relative preservation of the cartilage space, despite extensive bone involvement, is characteristic of this condition. If it is unrecognized, however, and allowed to progress for months or years, narrowing of the cartilage due to degeneration and hypertrophic bone formation will supervene and simulate osteoarthritis (Fig. 12*B*).

The diagnosis should be suspected in patients with rapidly developing "osteoarthritis," particularly if they have received steroid therapy. The roentgenologic distinction is usually not difficult. In osteonecrosis, sufficiently advanced to be confused with osteoarthritis, much of the femoral head is involved rather than only the subchondral portion and the bone changes precede the cartilage space narrowing, whereas the converse is usually true in osteoarthritis. Furthermore, the zones of rarefaction are not as discrete or rounded as in osteoarthritis and the adjacent sclerosis is fuzzy and not as sharply marginated. Although some compression of the subchondral bone often develops in osteoarthritis, generalized crumbling, collapse and large bite-like subchondral defects are distinctly unusual.

SUMMARY

Attention is called to the various roentgenologic manifestations of osteonecrosis. These include a subtle diffuse mottling of the bone, periosteal bone apposition along the femoral neck, isolated patches of sclerosis, irregular discrete rarefactions with fuzzy marginal sclerosis, the "rim sign," the "bite sign," subchondral cortical depression, generalized subchondral fragmentation and possibly acetabular protrusion. The so-called "steroid arthropathy" may in some, if not most, instances represent unrecognized aseptic necrosis. The signs and symptoms of osteonecrosis are non-specific and the clinical diagnosis rests largely with the radiologist. This diagnosis should be considered in patients who have "rapidly developing osteoarthritis," particularly in young individuals and in those who have received steroid treatment. A number of clinical conditions appear to be associated with aseptic bone necrosis but the nature of these relationships and the pathogenesis of the bone lesions are not well understood.

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VOL. 106, No. 3

ATROPHIC ARTHROPATHY AND DIABETIC NEURITIS*

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With improved long-term management, diabetes is becoming a leading cause of atrophic destructive arthropathy.

"DIABETIC osteopathy" is being reported with increasing frequency in the literature.[1,4,9] Review of the published illustrations reveals a mixture of diverse roentgenographic changes. These may reflect etiologies as diverse as infection, ischemia and neuropathy. Absorption, erosion and disappearance of bone alternate with osteosclerosis, periosteal proliferation, fragmentation and sequestration.

Such a wide spectrum of lesions is entirely compatible with the pathophysiology of diabetes. Atherosclerosis, ulceration, gangrene, cellulitis, osteomyelitis and peripheral neuritis are well known complications of this disease, each one alone being capable of producing bone changes demonstrable on roentgenograms. The roentgenographic picture of diabetic osteopathy, which is actually an osteoarthropathy, varies considerably depending on how many of these factors act upon a given joint.

The purpose of this paper is to describe a purely atrophic resorptive arthropathy occurring in 6 patients with diabetes mellitus and peripheral neuropathy, and to report on its long-term follow-up. Nearly all the lesions were encountered in the upper extremities, whereas most of the lesions of diabetic osteoarthropathy heretofore reported affected the lower extremities.

TERMINOLOGY

The terms: atrophic arthropathy, atrophic resorptive arthritis, atrophic destructive arthropathy (or arthritis), atrophic mutilating arthropathy, and arthritis mutilans are used interchangeably in the following report. Whenever neuritis or neuropathy is the salient point, the word "arthropathy" is replaced by "neuroarthropathy."

MATERIAL

The New York Medical College Center for Chronic Disease is an 1,800 bed hospital for the care and rehabilitation of the chronically ill. Patient ages range from 3 to 103 years, with the majority between 60 and 90 years. Both sexes are equally represented.

Arthritis mutilans was found in 17 patients. After eliminating 6 patients with rheumatoid arthritis and 5 with rheumatoid arthritis *and* diabetes, there remained 6 non-rheumatoid diabetics in whom diabetes was considered the possible cause of the arthropathy. Of these, 4 are classed as "pure" diabetics while 2 are considered "mixed." The definition of these 2 groups will be given later.

In this connection, it is noteworthy that 65 per cent (11 of 17) of all patients with atrophic destructive arthropathy were diabetics, whereas the incidence of diabetes in the hospital population at large is only 21 per cent.

ASSOCIATED DISEASES

Four of our 6 non-rheumatoid diabetics were females, 2 males. All exhibited signs of peripheral neuropathy. With one ex-

* Presented under the title "Diabetic Neuroarthropathy with Long-Term Follow-Up" at the Sixty-ninth Annual Meeting of the American Roentgen Ray Society, New Orleans, Louisiana, October 1–4, 1968.
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ception,* their ages were in the 61–86 year range. It is not surprising, therefore, that most of our patients were afflicted with more than one disease. The associated pathologic conditions were: peripheral vascular disease of the lower extremity—3 cases—with successful sympathectomy in one and unsuccessful sympathectomy in another; hyperuricemia without clinical evidence of gout—2 cases; Ehlers-Danlos syndrome—1 case; cirrhosis of liver, alcoholism, malnutrition and anemia—1 case (Case VI); Werner's syndrome (premature aging)—1 case (Case V); osteoarthritis of spine—2 cases; osteoporosis of spine—1 case; and scoliosis of spine—1 case.

For this reason, Cases V and VI were classed as "mixed" diabetics, since it was impossible to rule out alcoholic neuritis and Werner's syndrome as the cause of the arthropathy here, although these possibilities were considered remote. The remaining 4 patients were categorized as "pure" diabetics in the sense that no other of their concurrent diseases could be made responsible for their arthropathies.

None of our patients had any of the following diseases which are commonly regarded as possible causes of arthropathies of the type to be presented here:

Rheumatoid arthritis
  Negative history
  Negative physical findings
  Negative latex fixation test
  Absence of rheumatoid nodules
Neurosyphilis
  Negative history
  Negative VDRL test
Syringomyelia
Traumatic cord disease
Multiple sclerosis
Psoriasis
Raynaud's disease
Scleroderma
Infection, general or local, including leprosy
Clinical gout
Frost bites
Burns

* This patient, a 38 year old male, had Werner's syndrome (premature aging) and therefore is the equivalent of an older person.

Skin ulcerations over or near affected joint
The serum calcium and phosphorus levels were within normal range in all patients
The alkaline phosphatase was elevated in 1 patient
The uncorrected sedimentation rate was normal in 4 patients.

ROENTGENOGRAPHIC DEFINITION

The term atrophic arthropathy, or arthritis mutilans, as used here, denotes a joint condition which exhibits, on roentgenograms, osteoporosis, atrophy, destruction (*i.e.*, disappearance of bone substance, "erosion" etc.) and sometimes dislocation. To qualify, the joint must be free of osteophytes, sclerosis, eburnation, fragmentation, or detritus, that is it must lack the criteria commonly attributed to the hypertrophic variety of Charcot's arthropathy.

ROENTGENOGRAPHIC CLASSIFICATION

In order to judge or tabulate progression of the disease, a grading system was adopted by the authors which depended on "mortar and pestle," "pencil in cup" and similar deformities which occurred in nearly

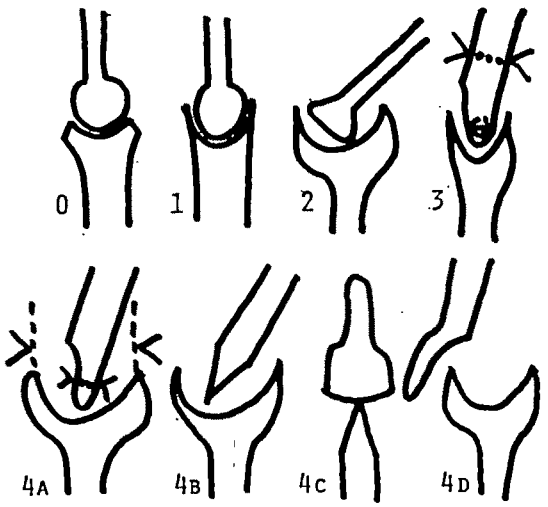


FIG. 1. Grading of deformity.
0 = Normal
1 = Intrusion
2 = Mortar and pestle
3 = Bulb < than shaft
4A = Bulb ½ of cup or less
4B = Pencil in cup
4C = Balancing pagoda
4D = Dislocation

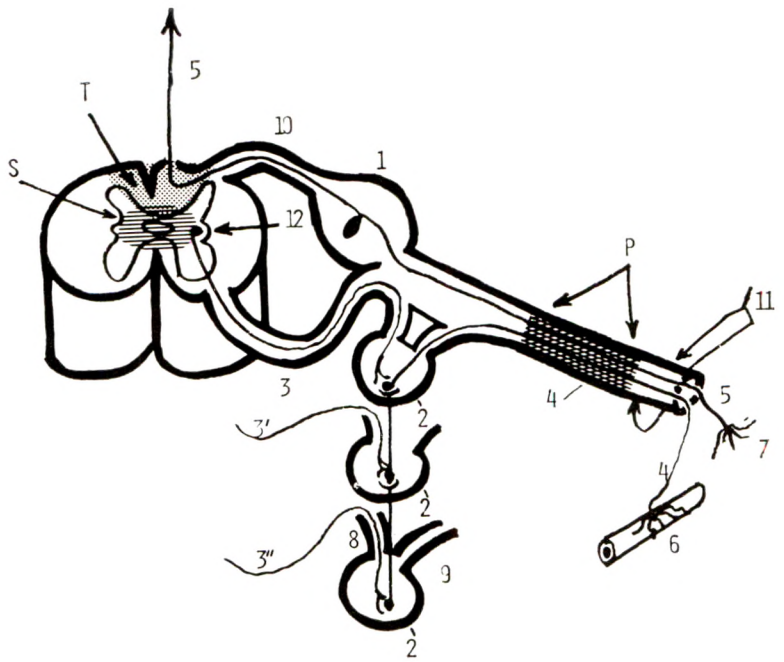


Fig. 2. Anatomic relationship between sensory fibers of a spinal nerve and the vasoconstrictive pathways of the sympathetic system.

1 = Dorsal root ganglion
2 = Sympathetic trunk ganglion
3 = Ventral root of spinal nerve
4 = Postsynaptic neuron of sympathetic nerve
5 = Sensory fiber of spinal nerve
6 = Vasoconstrictor
7 = Pain receptor
8 = White ramus communicans
9 = Gray ramus communicans
10 = Dorsal root of spinal nerve
11 = Spinal ("peripheral") nerve
12 = Intermediolateral horn
T = Structures affected by tabes dorsalis (dotted)
S = Structures affected by syringomyelia (hatched)
P = Structures affected by peripheral neuritis (crosshatched)

all affected joints. All deformities were caused by a whittling down process of the convex member and a gouging out or broadening of the concave member of the joint (Fig. 1), except in Case VI (Fig. 4) in which both opposed members became pointed.

ROENTGENOGRAPHIC FINDINGS AND PROGRESSION OF DISEASE

Long-term roentgenographic follow-up of 4 to 14 years was possible here in 4 cases. In the remaining 2, 1 year serial observation has been obtained thus far. The findings are summarized in Table 1.

As can be seen none of the arthropathies turned from an atrophic stage into a hypertrophic one or *vice versa*. This contradicts Brailsford's[2] opinion, according to which the atrophic arthropathy is merely the fourth stage of Charcot's arthropathy. Effusion was seen to precede the destructive joint changes in several instances, however, and—in this respect—our observations agree with those of Brailsford.

LOCALIZATION

Atrophic osteoarthropathy was en-

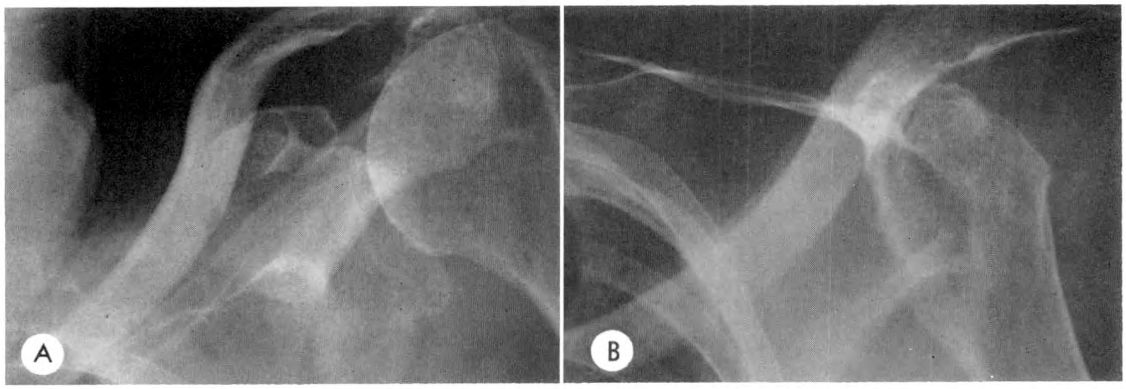


FIG. 3. Case IV. An 86 year old woman with diabetes and hyperuricemia but without clinical gout. (*A*) Left shoulder. Appearance in 1952. Except for small periarticular calcifications, no abnormality is demonstrated. (*B*) Left shoulder. Roentgenographic appearance in 1966. The humeral head has reduced to a small club-shaped protrusion and the glenoid fossa has enlarged. A subluxation is also present.

countered more often in the upper extremity than in the lower one and was absent from the spine, as shown in Table II.

DISCUSSION

Common to all patients was the presence of diabetes mellitus and peripheral neuropathy. The diagnosis of diabetes mellitus was based on a positive previous history and abnormal fasting blood sugar levels in 2, and on an abnormal glucose tolerance test in the remaining 4 cases. The blood glucose values were obtained from fresh venous blood and analyzed by the "true glucose" method with autoanalyzer technique. The criteria for diabetes mellitus were such as proposed by Fajans and Conn for subjects under 40 years of age, and also met—with one exception—the 1968 standards accepted by the American Diabetes Association for individuals over 60 years of age. All patients required a diabetic diet for maintenance. Two needed additional oral antidiabetic agents, whereas one had to



FIG. 4. Case VI. A 61 year old man with diabetes, alcoholism, cirrhosis of liver and malnutrition. A successful left lumbar sympathectomy for peripheral vascular disease of lower extremity was performed in 1956. Two years later, his left foot began to shrink. No sympathectomy had been performed on the right; his right foot remained normal in size. A roentgenogram of both feet taken in 1968 shows severe "whittling down" of metatarsal bones and proximal phalanges of the left foot resembling opposed pencils while there are only minor changes of atrophic arthropathy in the right foot.

TABLE I

SUMMARY OF CASES

Case	Sex	Age	Year	Shoulder		Elbow		Wrist		Hand		Hip		Knee		Ankle		Foot		Spine	Associated Diseases
				R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L		
I. J.A. (deceased)	F	82	1963 1964 1966 1967	o 3 4	o o+E 2 4	 2	 o					 o	 o		 o					Osteoarthritis, scoliosis	Biopsy, shoulder—no growth; PVD, lower extremity; cystic kidney
II. E.H.	F	78	1955 1956 1962 1964 1966 1967	o o	o o	 	 3 4 4 	 1 		 	 	 oF. 	 o 	 oC 	 o 	 o o 	 o o 	 o o 	 o o 	Osteoporosis	Hyperuricemia
III. C.S.	F	71	1959 1960 1967	 o	 o	4 4 4	3Fx 3/4 4	 o	 o	 o	 o	 4	 4	 o	 o	 o	 o	 o	 o		Ehlers-Danlos syndrome
IV. M.J.	F	86	1952 1953 1955 1956 1958 1961 1964 1965 1966 1967	o o 1 1 	o 1 2 3 	 2 2/3 3	 o 3	 2 2/3 3/4	 2 3 3/4	 1 1 2 3	 o 2 2	 o o 	 o o 	 1 2 	 1 2 					Osteoarthritis	Hyperuricemia
V. W.L.	M	38	1967 1968	o	o	 	2 2	o	S.F.	o	oC	o	o		oC				oC		Werner's syndrome; unsuccessful bilateral sympathectomy for PVD of lower extremity
VI. C.P.	M	61	1967 1968		oFx	 	 	o	o	o	o	o	o			o	o	o/1 o/1	4 4		Anemia; malnutrition; cirrhosis of liver; chronic alcoholism; PVD; sympathectomy in 1956

PVD = peripheral vascular disease; E = effusion; C = contracture; S.F. = surgical fusion; F. = fusion, Fx = fracture.

TABLE II

ANATOMIC DISTRIBUTION OF ATROPHIC DESTRUCTIVE ARTHROPATHY IN 6 PATIENTS

Shoulders	2 cases
Elbows	5 cases
Wrist or hand	2 cases
Hip	1 case
Knee	1 case
Foot	1 case

take 40 units of insulin daily in the past but is now able to manage on a diabetic diet alone.

Peripheral neuropathy was diagnosed on the basis of decreased tendon reflexes, paresthesia, decreased vibration sense, decreased pin-prick sensation and decreased position sense. All affected joints were painless on passive or active motion.

Finally, we would like to speculate on the mechanism that distinguishes this disease from the hypertrophic variety of Charcot's arthropathy.

The hypertrophic arthropathy is usually associated with a lesion in the posterior tracts (as in tabes) or the central portion of the gray matter of the spinal cord (as in syringomyelia). Such lesions exempt the sympathetic system by virtue of their anatomic location (with certain exceptions).

In peripheral neuropathy, however, the spinal nerve is affected. It contains sympathetic fibers in addition to sensory and motor ones. They normally carry vasoconstrictive impulses. When the function of the postganglionic peripheral nerve is damaged, however, two events will take place: (1) loss of protective pain sensation will lead to mechanical overuse of the joint; and (2) loss of vasoconstrictive impulses will lead to hyperemia.

Only when both events combine, does the atrophic variety occur. A case in point is patient C. P. (Case VI). Here, severe joint changes occurred in the left foot 2 years after a successful left sympathectomy. No sympathectomy had been performed on the right and the right foot showed only minor changes attributable to diabetic arthropathy. One is inclined, therefore, to judge the ultimate effect of peripheral diabetic neuropathy upon a given joint according to whether or not an "autosympathectomy" has occurred.

Figure 2 shows the anatomic relationship between the sensory fibers of a spinal nerve and the vasoconstrictive pathways of the sympathetic system. Tabes dorsalis affects chiefly the posterior columns of the spinal cord (dotted area) and syringomyelia mainly the central portions of the gray matter, particularly the posterior horns and the peri-ependymal regions of the cord (hatched area).

Peripheral neuropathy on the other hand attacks the postganglionic sections of the nerve and is thus capable of inactiv ting sensory as well as sympathetic fibers (cross-hatched area).

The concept is not new. Leriche[6] postulated it and attributed neurogenic bone absorption to a lesion of the sympathetic nerve leading to hyperemia. On a clinical level, this hypothesis lent support by Klümper *et al.*[5] who recently reviewed 49 patients with traumatic peripheral nerve injury of the lower extremities, 11 of whom developed resorptive arthropathy.[5] On an experimental level, this concept is expressed by Shim[10] who has shown that peripheral nerve section causes hyperemia of bone in animals. He cites others who produced the same effect by lumbar sympathectomy in dogs.

Syringomyelia extends occasionally into the intermediolateral horn region (Fig. 2) which contains sympathetic centers. Even then, however, it cannot prevent vasoconstrictive impulses from reaching the peripheral arteries because the chain of sympathetic trunk ganglia supplies an alternative pathway there.

In this connection, it is well to consider some of the clinical differences between the hypertrophic and the atrophic type of Charcot's arthropathy. The hypertrophic type is usually associated with spinal cord disease, such as tabes dorsalis, syringo-

myelia and spinal cord trauma. The lower extremities are more often involved than the upper ones here, and the spine is also often affected. The term "Charcot's spine" has—as a matter of fact—become a hallmark of this disease. In our total series of atrophic arthropathy, regardless of cause, the incidence of upper extremity involvement was 5 times as high as that of the lower extremities; moreover, the spine was never involved.

Why there is a predominance of upper extremity joint involvement in our series is difficult to state. Nearly all our patients are wheelchair dependent and over-use their arms while under-using their legs. Although diabetic neuritis *per se* was thought to have a predilection for the lower extremities, Ellenberg[3] reported recently 35 cases of upper extremity diabetic neuropathy collected in the past 5 years.

CONCLUSION AND SUMMARY

With improved long-term management, diabetes is becoming a leading cause of atrophic destructive arthropathy.

Six non-rheumatic diabetic patients with severe atrophic joint changes were observed who were followed roentgenographically for 1 to 14 years. Progression of the disease from a normal joint to severe destruction was demonstrated in 2 patients, whereas in the other 4, destruction was present when they were first roentgenographed.

Common to all was the presence of diabetic neuropathy and the absence of other conditions likely to be responsible for the joint changes, with two partial exceptions noted.

Attention is focused upon the lack of hypertrophic changes commonly expected in Charcot's arthropathy. The authors postulate that the atrophic type is caused by a peripheral neuritis leading to an "autosympathectomy" in addition to impairment of the sensory fibers. Only when hyperemia and loss of protective pain sensation combine can the atrophic variety occur.

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TOMOGRAPHY OF THE OPTIC CANAL*

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THE optic canal leads from the middle cranial fossa posteriorly to the orbit anteriorly. The axis of the optic canal passes laterally from posterior to anterior forming an angle of 37° with the midsagittal plane (Fig. 1*A*). The axis of the optic canal also proceeds inferiorly from posterior to anterior forming an angle of 30° with Reid's baseline (Fig. 1*B*).[2,3]

Therefore, in order to place the optic canal at right angles to the film, the head must be rotated 37° and elevated 30°. This positioning is difficult to achieve consistently and to hold steady for the 20 minute tomographic examination of the optic canal.

METHOD

A device which helps in positioning the patient correctly and at the same time helps him to hold the position is the V board designed by Pfeiffer in 1933[4] (Fig. 2). This board consists of 2 hinged pieces of plastic held apart by an elevated forehead rest. The angle between the pieces of plastic is 106°. Therefore, if the patient is put in a prone position with the nose pointing toward the crotch of the V in the midsagittal plane bisecting the V, the head would automatically be rotated 37°. Also, the elevation upon which the forehead rests is just high enough so that when the patient's forehead is resting on it, the head is extended 30°.

The centering light is then placed 7 cm. superior to the top of the external ear and in line with the lateral canthus. The patient is now in position, with the optic canal at right angles to the film and in the center of the field. The patient also has a positive

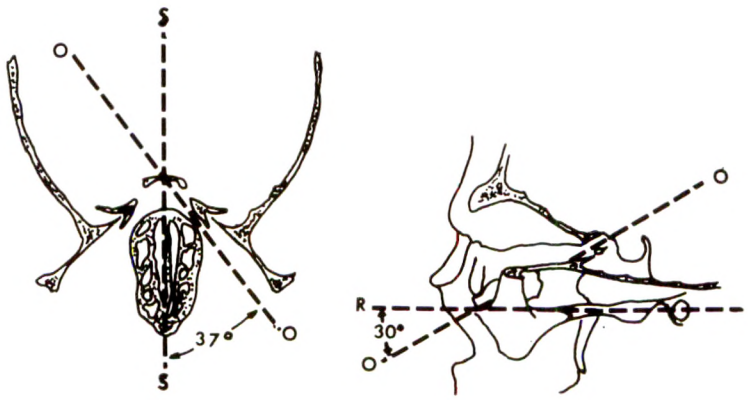


FIG. 1. Schematic drawing showing the angles formed by the axis of the optic canal. (*A*) Axial view. O-O = axis of the optic canal; S-S = midsagittal plane. The axis of the optic canal passes laterally from posterior to anterior forming an angle of 37° with the midsagittal plane. (*B*) Lateral view. O-O = axis of optic canal; R = Reid's baseline. The axis of the optic canal passes inferiorly from posterior to anterior forming an angle of 30° with Reid's baseline.

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rest which makes it easier for him to hold the position for 20 minutes.

A conventional optic canal view is then taken to ensure that the positioning is correct (Fig. 3*A*). The conventional optic canal view is achieved by disconnecting the tomographic apparatus so that the tube does not move.

Scout tomograms at 7, 7.5, and 8 cm. from the tabletop are obtained (Fig. 3, *B* and *C*). These scout tomograms make it possible for the radiologist to designate the exact sections that are necessary to encompass the entire optic canal from its cranial end to its orbital end at 1 mm. intervals. Since the average optic canal is 7 mm. in length, the entire optic canal can be encompassed on two 10×12 inch films with 6 tomographic sections on each film.

Some writers[1,6] advocate optic canal tomograms at every 5 mm. This is not sufficient. If the section interval in optic canal tomography is 5 mm., only one section of the optic canal will be obtained and since this one section could fall on any part of the canal from its cranial end to its orbital end, it would be impossible to evaluate its size or shape in relation to other sections of the same canal or for comparison with the opposite canal. Therefore, we suggest a section interval of 1 mm. when tomographing the optic canals.

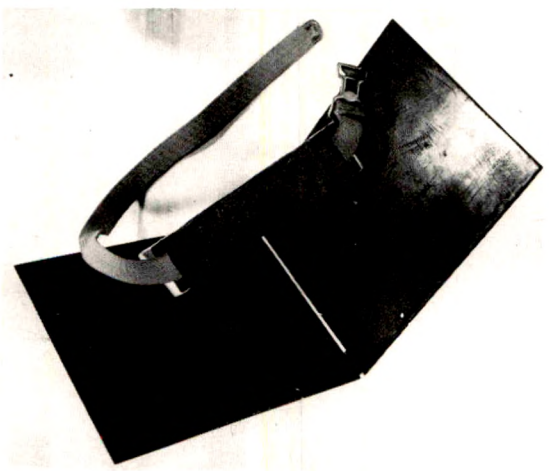


Fig. 2. The "V" board used to position the patient for optic canal tomography.

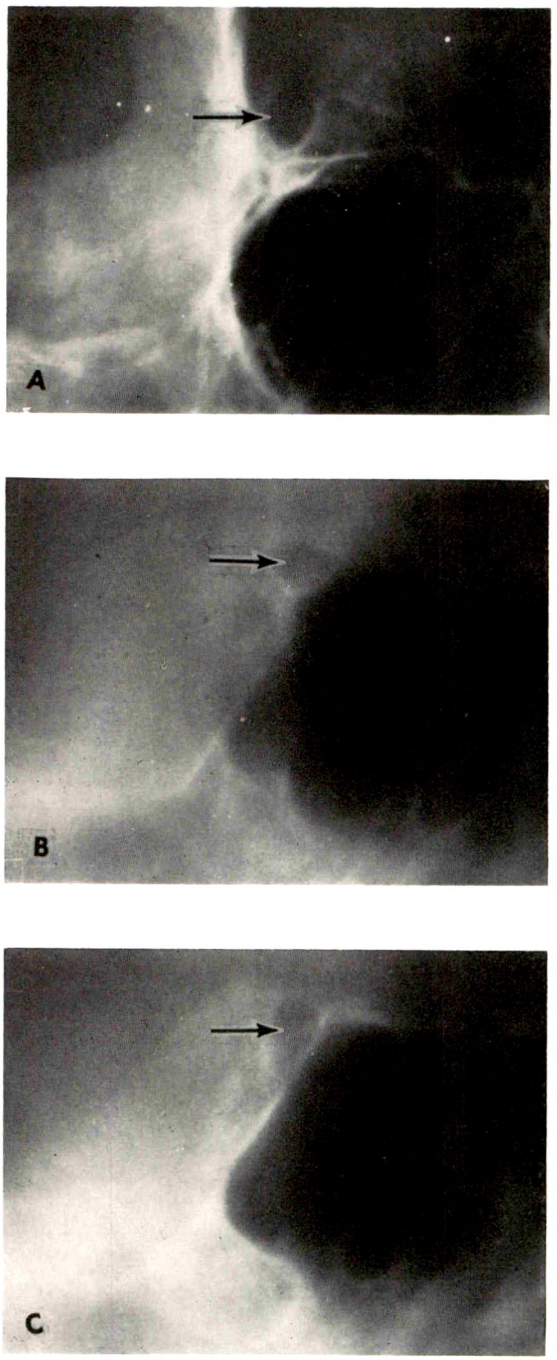


Fig. 3. Scout roentgenograms taken in preparation for tomographic examination of the optic canal. (*A*) Conventional optic canal view showing the optic canal (arrow) in its proper position in the inferior lateral quadrant. (*B*) Scout tomogram of optic canal 8 cm. from the tabletop at the cranial end of the optic canal (arrow). (*C*) Scout tomogram of optic canal 7.5 cm. from the tabletop at the orbital end of the optic canal (arrow).

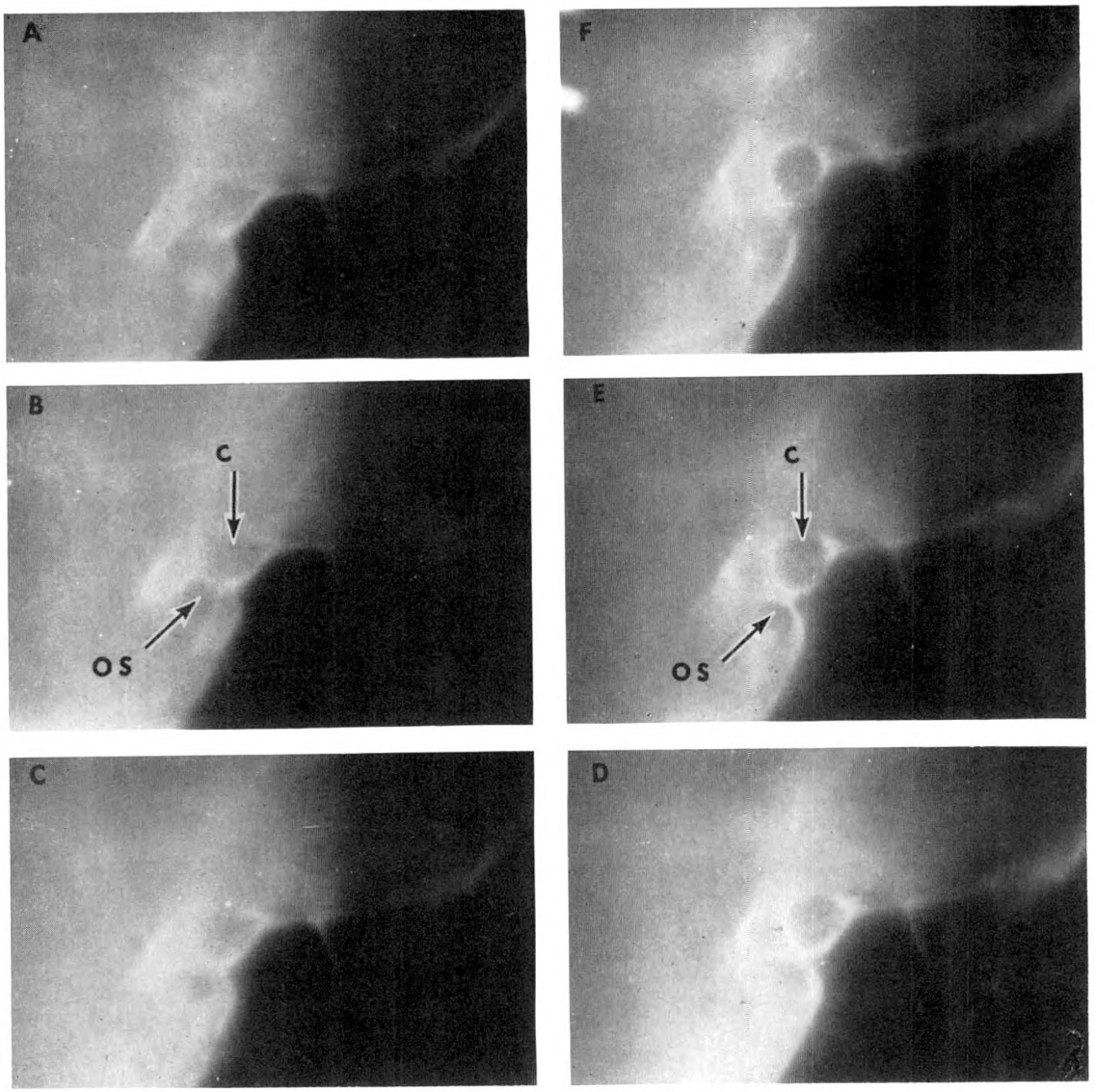


FIG. 4. Six tomograms of a normal optic canal on one 10×12 inch film. C = optic canal; OS = optic strut. These tomograms go from the cranial end of the optic canal (*A*) by 1 mm. intervals to the orbital end (*F*). The shape of the canal changes from one section to the next. The cranial end of the canal (*A*) is oval with the long axis horizontal. The midportion of the canal is round (*D*). The orbital end of the canal is oval but with its long axis vertical (*F*). The walls of the canal, especially the optic strut, are denser and heavier on the orbital end than on the cranial end.

NORMAL TOMOGRAPHIC ANATOMY

The shape of the canal continuously changes from one section to the next: the cranial end of the canal is oval with its long axis horizontal (Fig. 4*A*); the midportion of the canal is almost round (Fig. 4*D*); and the orbital end of the canal is again oval but with its long axis vertical (Fig. 4*F*).

The optic strut which forms the inferolateral wall of the canal is thicker and heavier on the orbital end than on the cranial end. The more dense orbital end of the canal is the section which dominates the optic canal image on routine studies. That is why the image which is demonstrated in Figure 4 in the tomographic section of the orbital end of the optic canal is familiar, as it is the image which is generally seen on routine optic canal views.

The image on the routine optic canal

views does not resemble the horizontally oriented oval of a section of the cranial end of the optic canal. A considerable portion of the posterior cranial end of the canal can be distorted or destroyed and not affect the appearance of the canal on routine optic canal views.

To demonstrate the normal anatomy, we positioned a cadaver head and took transverse optic canal tomograms at every 1 mm. interval. Without changing its position, the specimen was then sawed at 2 mm. intervals, so that we obtained one 1 mm. thick slice at every second millimeter, the other millimeter of tissue being lost to the saw blade. Therefore, we obtained a total of 3 anatomic slices of the optic canal, each one being 1 mm. thick. We made a contact radiograph of each slice (Fig. 5, *A*, *B* and *C*). The roentgenogram of the specimen is comparable to the tomogram because the hypocycloidal tomogram has a 1 mm. focal plane thickness and the anatomic slice is also 1 mm. thick.

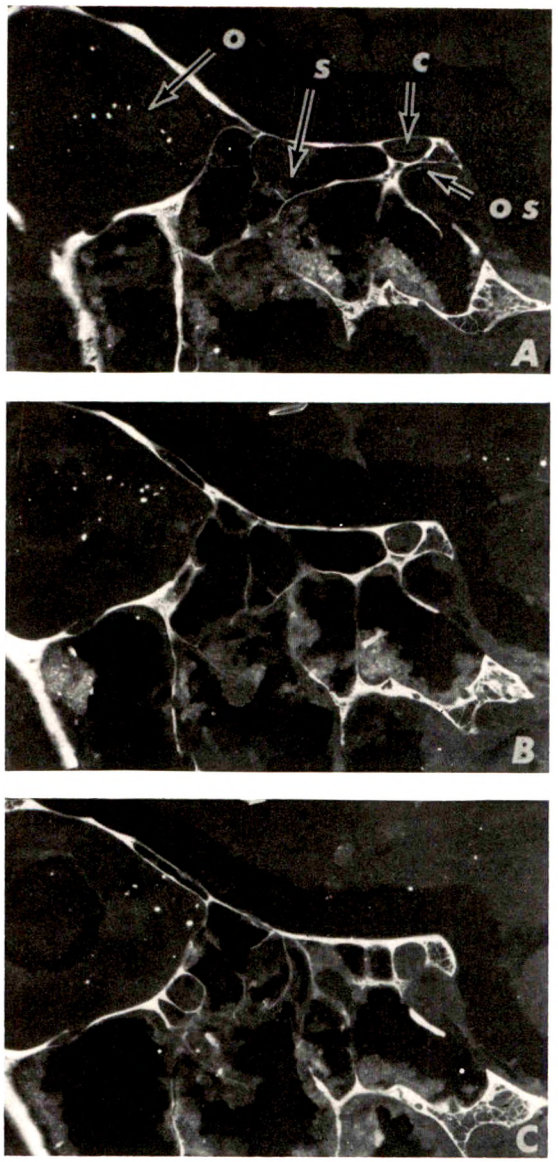


Fig. 5. Anatomic sections of the optic canal sliced in the same orientation as for optic canal tomograms. O = opposite orbit; S = sphenoid sinus; C = optic canal; OS = optic strut. (*A*) Section of the cranial end of the optic canal. Note the horizontal oval of the optic canal (C). (*B*) Section of the midportion of the optic canal. The canal is more round. (*C*) Section through the orbital end of the canal. The canal is a vertical oval.

Pathologic optic canals

As a matter of course, routine optic canal views are taken on all patients who have visual defects. When the optic canals are abnormal, we recommend tomography. In addition, we recommend tomography even when the routine views appear normal in cases of otherwise unexplained vision loss and vision loss after trauma to the orbit.

We performed tomography with the V board method on both optic canals of 50 patients. In this series of 100 optic canals, there were 70 normal canals and 30 abnormal canals; 23 patients had bilaterally normal canals. Abnormal canals on one or both sides were found in 27 patients (Table 1).

Unexplained vision loss

A case of unexplained vision loss was that of a 10 year old boy who had progressive right vision loss for 2 years. His routine optic canal views appeared normal (Fig. 6, *A* and *B*). Tomograms were taken.

The cranial end of the right optic canal (Fig. 7*A*) was markedly larger than was the cranial end of the left (Fig. 7*B*). But the orbital end of the right optic canal (Fig. 7*C*) appeared the same as the orbital end of the left (Fig. 7*D*).

We reported it as probable optic glioma[5] affecting the optic canal only on its cranial end. This was confirmed at surgery. The fact that the orbital ends of the 2 canals

TABLE I

PATHOLOGY IN OPTIC CANALS

8	Optic glioma
4	Fracture
3	Fibrous dysplasia
3	Meningioma
3	Dural calcification
2	Sphenoid tumor
1	Mass in sella
1	Congenital hypoplasia
1	Craniometaphyseal dysplasia
1	Calcification of optic nerve
27	Patients with abnormal optic canals

were normal explains why the optic canal in the routine optic canal views appeared normal, even though in reality the right optic canal was grossly abnormal. This is because, as we have noted, the image of the optic canal on routine optic canal views is dominated by the thicker and more densely calcified walls of the orbital end.

VISION LOSS AFTER ORBITAL TRAUMA

After trauma to the orbit, unexplained loss of vision of the involved orbit is not uncommon. This is usually ascribed to "avulsion" of the optic nerve. Actual fractures of the optic canal are seldom seen. In our series, 4 patients had vision loss after trauma to the orbit. By means of tomography of the optic canal, a fracture was demonstrated in every case. None of these fractures were revealed on routine optic canal views. Figure 8 demonstrates a section through the optic canal in one of these cases. The fracture line is seen to extend through both the superior and inferior walls of the optic canal.

SUMMARY

To obtain accurate transverse tomograms of the optic canal, we have adapted a special V board to help position the patient correctly and aid him to hold this position.

In order to locate an abnormality of the optic canal, and in order to compare one portion of one canal to the corresponding portion of the opposite canal, we recommend a tomographic section interval of 1 mm.

Tomography of the optic canals is suggested in patients who have abnormal optic canals on routine roentgenographic studies and also in cases of otherwise unexplained vision loss or vision loss after trauma. We have tomographed the optic canals of 50 patients, 27 of whom had abnormal optic canals.

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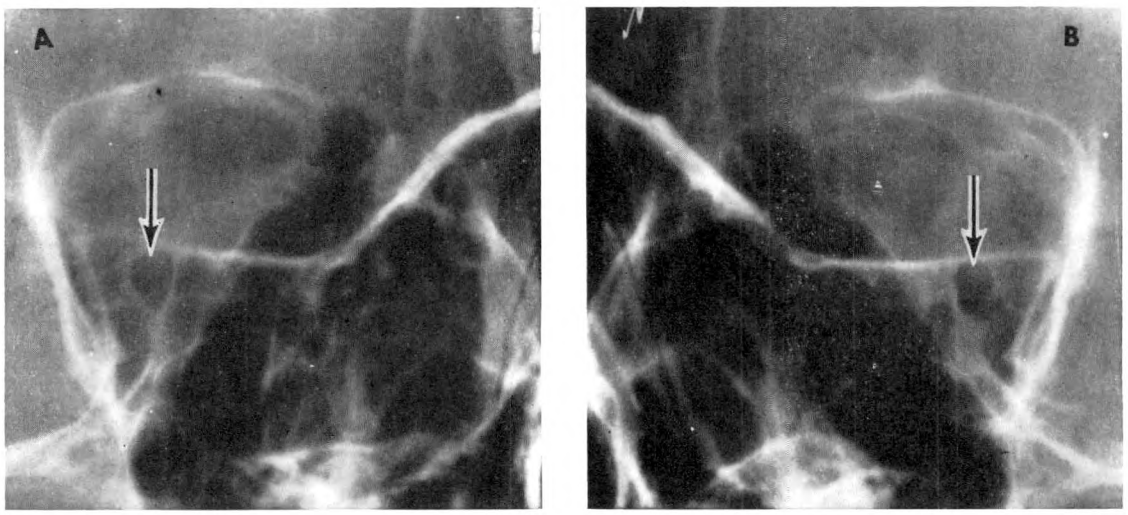


FIG. 6. Routine optic canal views in a patient with a right optic nerve glioma for 2 years. The optic canal (arrow) appears normal. (*A*) Right optic canal. (*B*) Left optic canal.

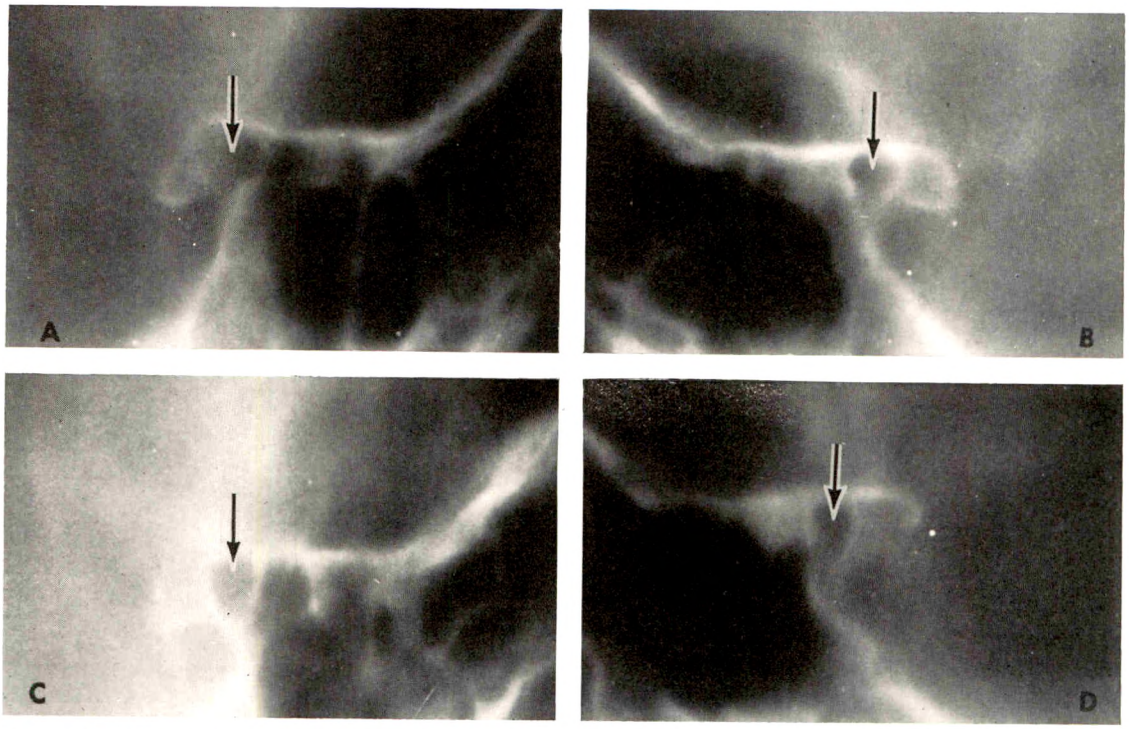


Fig. 7. Tomograms of the optic canal of the same case as in Figure 6. (*A*) Cranial end of the right optic canal. (*B*) Cranial end of the left optic canal. (*C*) Orbital end of the right optic canal. (*D*) Orbital end of the left optic canal. The cranial end of the right optic canal is markedly larger than the cranial end of the left, but the orbital ends of the canals appear symmetrical. The optic canal is affected only on the cranial end, leaving the orbital ends of the canal normal.

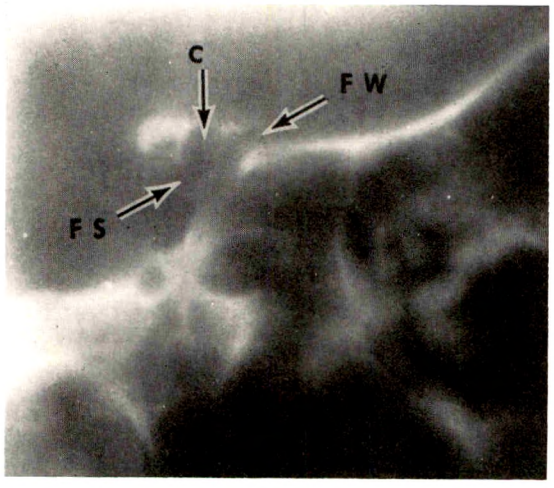


Fig. 8. Fracture of the optic canal as shown by tomography. C = optic canal; FS = fracture of the optic strut; FW = fracture of the superior wall of the optic canal. The fracture extends through the optic canal so that the superior lateral portion is completely detached.

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SELECTIVE CORONARY ARTERIOGRAPHY*

A SPOT FILM ROENTGENOGRAPHIC TECHNIQUE

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THE coronary vessels are presently examined by means of 2 basic roentgen procedures, cinefluorography and direct serial roentgenography.[1,2,4–8] As a rule, cinefluorography and direct serial roentgenography are complementary rather than competitive basic techniques.[3] In our experience with 1,200 cases, cinefluorography gives an unexcelled appreciation of the dynamics of the heart and coronary vessels. The entire circulation can be surveyed with surprisingly good anatomic detail. However, there are limitations of the image intensifier, particularly with the large patient. Because of this we have used direct roentgenography by a spot film technique in 400 patients in addition to the 35 mm. cine films. A single roentgenogram can provide a wealth of anatomic detail (Fig. 1, *A-F;* 2, *A-D;* 3, *A-D;* and 4, *A*, *B* and *C*).

In reasonably skilled hands the tip of the Sones catheter can consistently be placed in both coronary arteries and spot films exposed at the end of an injection. The right coronary artery has been visualized by direct roentgenographic technique in 100 per cent of the patients. The success rate of the left coronary artery opacification has been approximately 95 per cent. The purpose of this paper is to outline the spot film roentgenographic technique, using the Sones approach.

MATERIAL AND METHOD

Over 10,000 contrast medium injections were filmed by cinefluorography in 1,200 patients studied for suspected coronary artery disease. Direct roentgenography by spot filming was used in the last 400 patients. A Sones Type I, 80 cm., No. 8 F catheter was employed in all cases. It provides a stiff shaft for good catheter control, and a flexible tip enabling direct coronary artery catheterization.

RIGHT CORONARY ARTERY

A right brachial arteriotomy is performed and a Sones Type I catheter is introduced in a retrograde fashion into the ascending aorta just above the aortic valve. With the patient in the left anterior oblique position a small test injection is made to outline the right coronary ostium. With a constant rotation, either in a clockwise or counterclockwise direction, the right coronary artery is easily catheterized. Blood pressure and the electrocardiogram are constantly monitored. The right coronary artery is first visualized on the cine film. This enables the operator to position the patient properly for a single spot film roentgenogram. Ordinarily, the best position for the spot film roentgenogram is in the left anterior oblique projection, 45° from the supine. The catheter rests easily in the proximal segment of the right main trunk (Fig. 1*A*). The exposure is made at the end of the coronary artery injection. This usually requires 2 to 3 cc. of contrast medium (70 per cent hypaque mixture). The right coronary artery is then studied in the right anterior oblique projection. The tip of the Sones catheter can be left in place if the patient is on a rotating cradle. With the patient positioned in the right anterior

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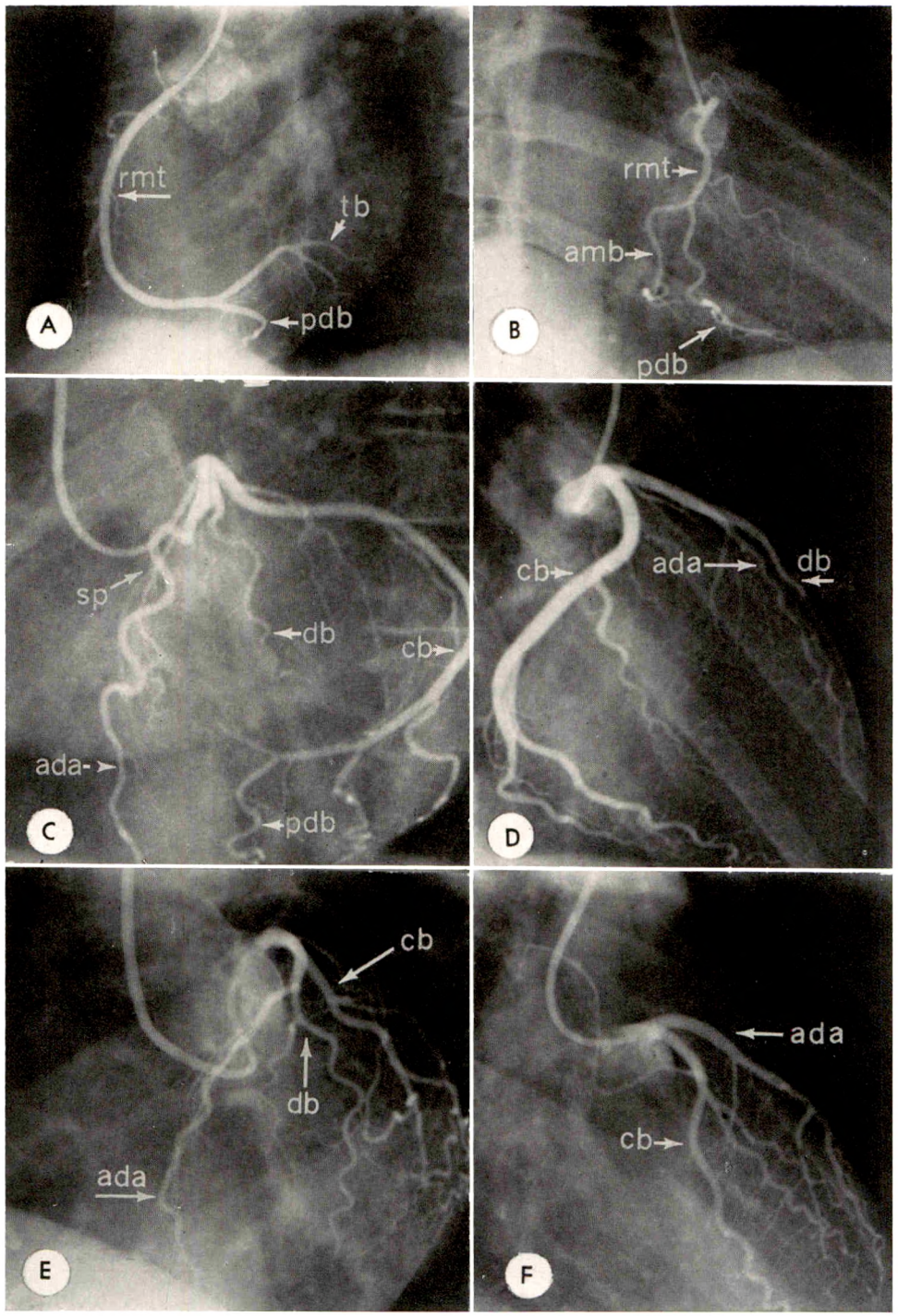


FIG. 1. Spot roentgenograms of selective contrast agent injections in the right and left coronary arteries in the left anterior oblique and right anterior oblique positions. (*A*) Right coronary artery, left anterior oblique position. Right main trunk (rmt) is well seen. The posterior descending branch (pdb) is seen at the crux of the heart. A portion of the left ventricle is supplied by terminal branches (tb). (*B*) Right coronary artery, right anterior oblique position. The right main trunk (rmt), its acute marginal branch (amb), and

(*Legend continued on page 538*)

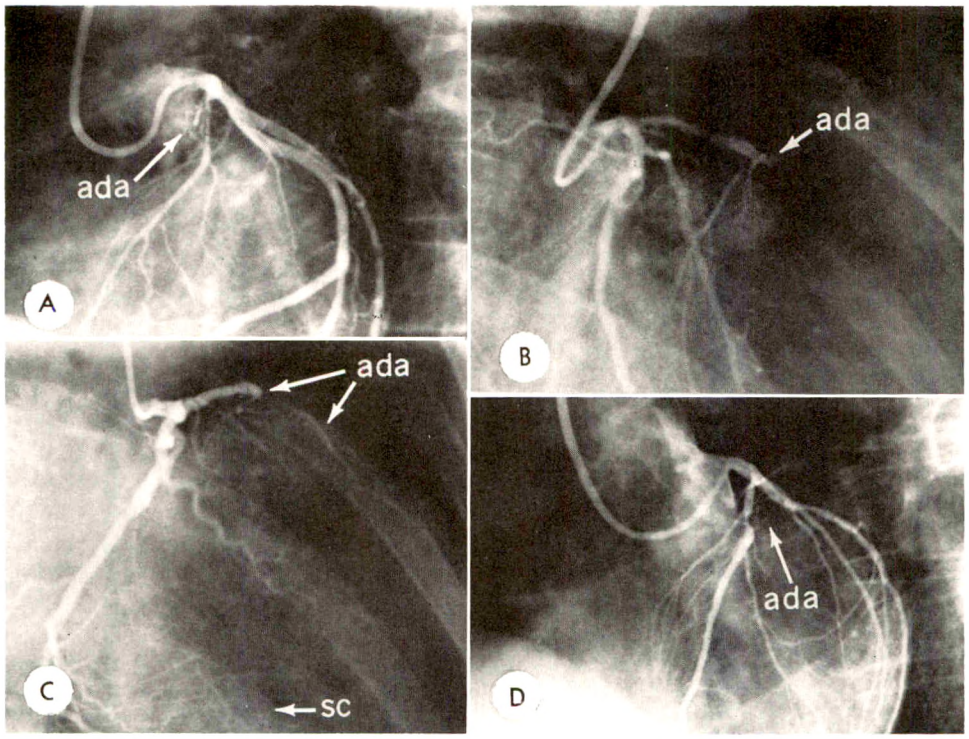


FIG. 2. Selective coronary arteriograms of 4 different patients—each with obstructive disease of the left coronary artery. (*A*) Left anterior oblique position, left coronary artery. There is an obstructive lesion in the proximal segment of the anterior descending artery (ada). (*B*) Right anterior oblique position, left coronary artery. Total occlusion of the anterior descending artery (ada) is demonstrated in a patient with a large anterolateral ventricular aneurysm. (*C*) Right anterior oblique position, left coronary artery. Small bridge collaterals with almost total occlusion of the anterior descending artery (ada) are shown. There are also extensive septal collaterals (sc). (*D*) Left anterior oblique positions, left coronary artery. There is almost total occlusion at the proximal segment of the anterior descending artery (ada).

oblique projection, approximately 20 to 30° from the supine, another spot film roentgenogram is taken (Fig. 1*B*).

LEFT CORONARY ARTERY

The catheter is rotated from the right coronary ostium and usually assumes one of two positions: either the tapered portion of the shaft is resting in the sinus of Valsalva (Fig. 1, *C* and *E*) or the tip is elevated directly into the proximal segment of the left main trunk (Fig. 1*F*). Again the cine film is exposed to judge the coronary pattern. Cinefluorography is used in 3 positions of the left anterior oblique—35, 45 and 60°. The spot film is exposed in the left anterior oblique position, 45°. This position clears the circumflex branches from the thoracic spine: 4–6 cc. of contrast medium is used and the film is exposed at the end of the injection. If a rotating cradle is used, the catheter tip remains in place and the

the posterior descending branch (pdb) are seen in profile. (*C*) Left coronary artery, left anterior oblique position. The major branches are demonstrated: anterior descending artery (ada), septal perforator (sp), diagonal branch (db), circumflex branches (cb) and posterior descending branch (pdb). (*D*) Left coronary artery, right anterior oblique position. The anterior descending artery (ada), circumflex branches (cb), and diagonal branches (db) are seen in profile. (*E*) Left coronary artery, left anterior oblique position. The anterior descending artery (ada), diagonal branch (db), and the circumflex branches (cb) are opacified. (*F*) Left coronary artery, right anterior oblique position. The proximal portion of the anterior descending artery (ada), and the distal circumflex system (cb) are well outlined.

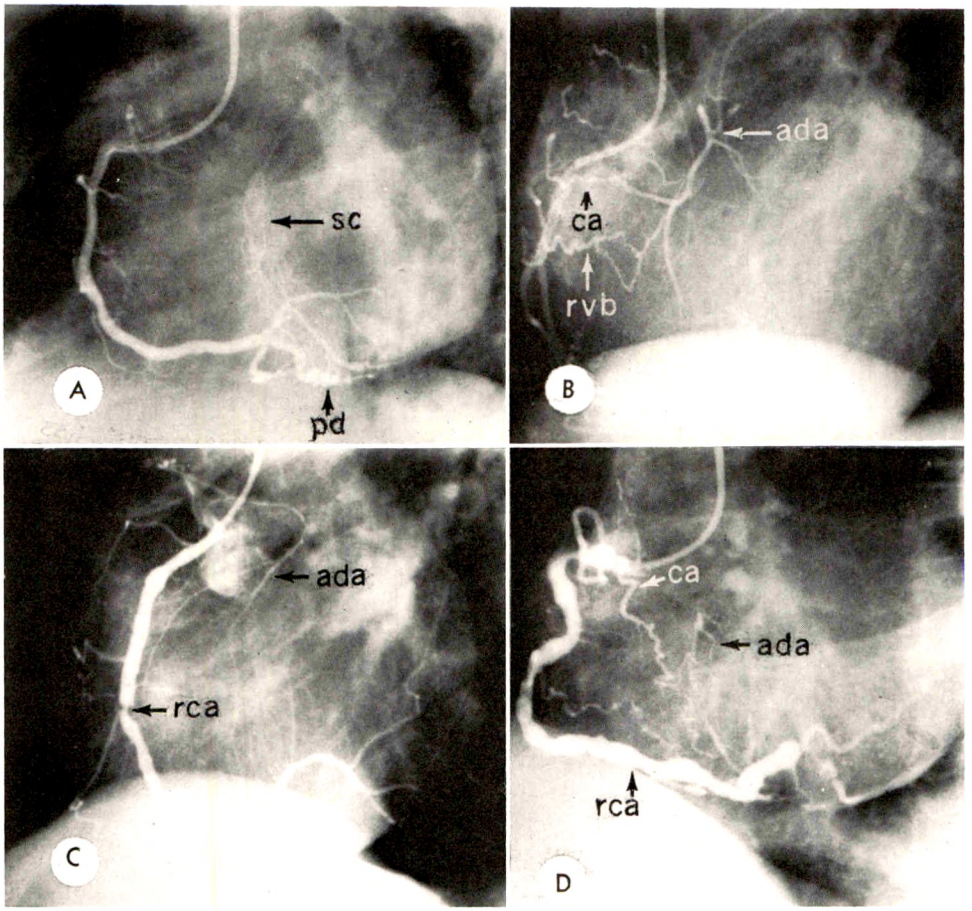


FIG. 3. Selective right coronary arteriograms. (*A*) Distal segment of the anterior descending branch fills via septal collateral vessels (sc) from the posterior descending branch (pd). (*B*) Opacification of the anterior descending artery (ada) to the point of obstruction via the conus artery (ca) and right ventricular branches (rvb) is demonstrated. (*C*) There is almost total obstruction of the right coronary artery (rca) at its mid portion. The anterior descending artery (ada) fills via collaterals from the proximal right coronary artery. (*D*) Diffuse obstructive disease with aneurysmal dilatation of the right coronary artery (rca). The prominent conus artery (ca) with collateral opacification of the anterior descending artery (ada) is shown.

patient is rotated to the right anterior oblique position, 15 to 30° from the supine.

A complete coronary study also requires left ventriculography to estimate myocardial contractility, and to exclude the possibility of ventricular aneurysm or mitral regurgitation. Ordinarily, the left ventriculography is done with the patient in the right anterior oblique position, 20 to 30° from the supine. The left ventricle is visualized using 35 mm. cine film.

TECHNICAL COMMENT

The spot film technique is based on the use of the manual spot film device with a 9–6 inch image tube. A size 10×12 inch, 10 to 1 ratio grid cassette with Kodak Royal Blue film is placed in the cassette holder beneath the image tube. All films are exposed in a single plane with a vertical beam. In our experience there was no problem with unacceptable magnification. The time exposure factor used was 1/40 of a second. The usual kilovoltage ranged from 80 to 100 at 300 ma., with a single phase generator. A 2 mm. focal spot with a Dynamax 50 (Machlett) roentgen-ray tube was used. Blurring does occur due to systolic cardiac motion, but in a surprisingly small percentage of the films; 35 mm. cineflure film,

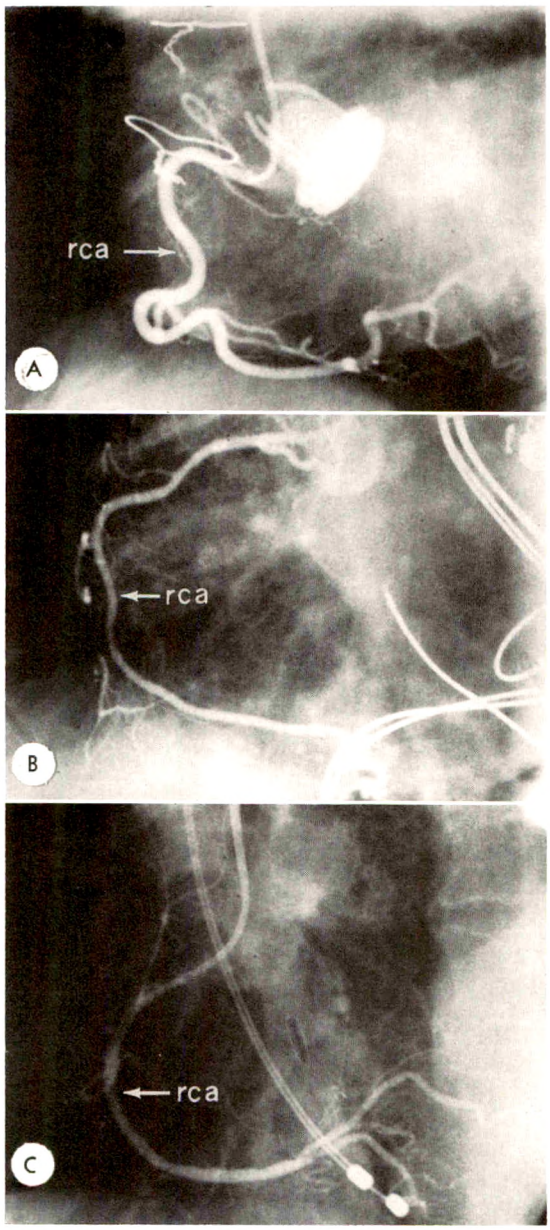


FIG. 4. Selective right coronary arteriograms of 3 different patients—Magovern aortic valve, myocardial electrode, transvenous endocardial electrode. (*A*) Left anterior oblique position, right coronary artery. This is a normal right coronary artery (rca) of a patient with a Magovern aortic valve. (*B*) Left anterior oblique position, right coronary artery (rca). A myocardial electrode is attached to the left ventricle. (*C*) Left anterior oblique position, right coronary artery (rca). The endocardial electrode is in the right ventricle.

Eastman-Kodak, is also exposed during the study. Usually 200 to 400 feet are used per patient. Four spot film roentgenograms are taken—2 of the right coronary artery and 2 of the left coronary artery.

DISCUSSION

Until now, selective coronary catheterization via the right brachial artery has been limited to cinefluorography. This is because Sones has insisted that the safety of the technique depends on constant visualization of the catheter tip and also careful monitoring of the aortic pressure and electrocardiogram. There has been some doubt as to the use of the Sones catheter with the serial roentgenographic technique, because of relative instability of catheter positions. We have found that the Sones catheter can be carefully placed in the right and left coronary artery with consistency and relative ease in a high percentage of the patients. The exposure of the single spot film requires only a brief period of nonvisualization of the catheter. In 400 consecutive cases there have been no episodes of ventricular arrhythmia, coronary artery dissection or myocardial infarction.

High quality selective spot films roentgenograms are the rule (Fig. 1–4). Movement blurring did occur in a small percentage of the patients but was kept to a minimum, possibly because the film was exposed when the patient performed the Valsalva maneuver and the contrast medium caused a sinus bradycardia. These two factors result in diminishing large and rapid movements of the heart. Because of this the exsisting generator and control apparatus can be arranged for satisfactory spot film roentgenograms. The use of the rapid changer can be avoided. Ideally, a 1,000 ma., 3 phase generator would enable the use of faster exposure times down to 1/120 second to further minimize blurring during systolic motion. Theoretically, it would also increase the range of the cine equipment and provide better cine film roentgenograms.

This roentgenologic technique does not replace cine photofluorography. Cine studies are unsurpassed in portraying the dynamics of coronary flow. However, the spot film method has practical advantages of direct roentgenography, including finer film detail and standard processing, filing and copying. A spot roentgenographic film can be processed quickly and the results observed. It is extremely helpful in a variety of circumstances when fine anatomic detail of the coronary arteries is required (Fig. 4, *A*, *B* and *C*).

This technique is based on the use of the Sones Type I catheter. In reasonably skilled hands both coronary arteries can be easily catheterized in multiple positions. The inconvenience of changing catheters and the possible complications of the percutaneous method are avoided. Open arteriotomy, with meticulous surgical technique under direct vision, used in our laboratory, has minimized intravascular stasis and injury.

SUMMARY

A new spot film roentgenographic technique has been devised to supplement the Sones method of selective cine coronary arteriography. There have been no complications in the first 400 cases using the combined procedure. The complete method is relatively simple, after one masters the manipulation of the Sones catheter. If a rotating cradle is used and the catheter is carefully positioned, both coronary arteries can be easily catheterized. The inconvenience of changing catheters is eliminated by the use of the Sones catheter, which is inserted into each coronary artery.

Cinefluorography and direct roentgenography by spot film technique can be conveniently combined with little additional expense. In our judgment the cine film is of prime importance because a greater amount of dynamic information is obtained; but the addition of spot film roentgenography is helpful in providing fine anatomic detail.

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CONGENITAL ABSENCE OF THE PERICARDIUM*

A REVIEW OF THE LITERATURE WITH DEMONSTRATION OF A PREVIOUSLY UNREPORTED FLUOROSCOPIC FINDING

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THE true incidence of congenital pericardial defects is unknown but it is more common than generally supposed. The number of cases reported in the literature has steadily increased in recent years as evidenced by 4 cases being reported from 1937 to 1939, 5 from 1940 to 1949, 21 from 1950 to 1959, and 57 from 1960 to 1967.

The purpose of this paper is to review methods of diagnosing congenital pericardial defects and to emphasize the pertinent roentgenographic and clinical findings. We analyzed 87 cases of congenital pericardial defects reported in the literature since the review of Southworth and Stevenson in 1938.[47] Fluoroscopic findings not previously reported will be discussed.

REPORT OF A CASE

A 20 year old male was referred to the University Hospital for cardiac evaluation. Nine months prior to admission, the patient was told that he had angina pectoris and corrected transposition of the great vessels after extensive cardiac evaluation.

Fifteen months previously he began having substernal chest pain. It was occasionally precipitated by exercise and radiated down the inner aspects of both arms; it was relieved in 45 seconds to 1 minute by nitroglycerin tablets.

Physical examination revealed a pulse of 84 per minute and a blood pressure of 120/60 mm. Hg. The remainder of the examination was normal except for the fact that the point of maximal cardiac impulse (P.M.I.) was diffuse and extended to the left of the anterior axillary line. No murmurs were heard.

A chest roentgenogram (Fig. 1*A*) suggested absence of the left pericardium, particularly in view of the absence of any valvular disease or pectus excavatum deformity. Fluoroscopy revealed a vertical line just to the left of the spine (Fig. 2*A*). This line was found to be separated several centimeters from the aorta on the cinefluoroscopic film.

An electrocardiogram showed right axis deviation. Left and right-sided catheterization and angiocardiographic studies were normal (Fig. 1*B*). The heart was, however, rotated clockwise with the left heart border being formed by the right ventricle. A diagnostic pneumothorax demonstrated abnormal passage of air to the right side of the heart (Fig. 1*C*).

Complete absence of the left pericardium was found at the time of thoracotomy. The surgeon noted that "the heart appeared to really hang on a pedicle consisting of the aorta and pulmonary artery." The free edge of the right pericardium was somewhat thickened and rolled up (Fig. 2*B*).

HISTORICAL REVIEW

Columbus[9] is credited with the original report of this defect in 1559. In 1936, Ladd[30] first observed pericardial defect by pneumothorax. Southworth and Stevenson[47] in 1938, reported the first case with adequate clinical and fluoroscopic findings. Sunderland and Wright-Smith[48] in 1944 reviewed the embryologic theories of the pericardial defects. From experimental work on dogs in 1953, Moore and Shumacker[32] concluded that pericardium serves no useful function. Ellis, Leeds and Himmelstein[15] in 1959 reviewed the roentgenologic aspects of the pericardial defects and described the first case diagnosed by chest

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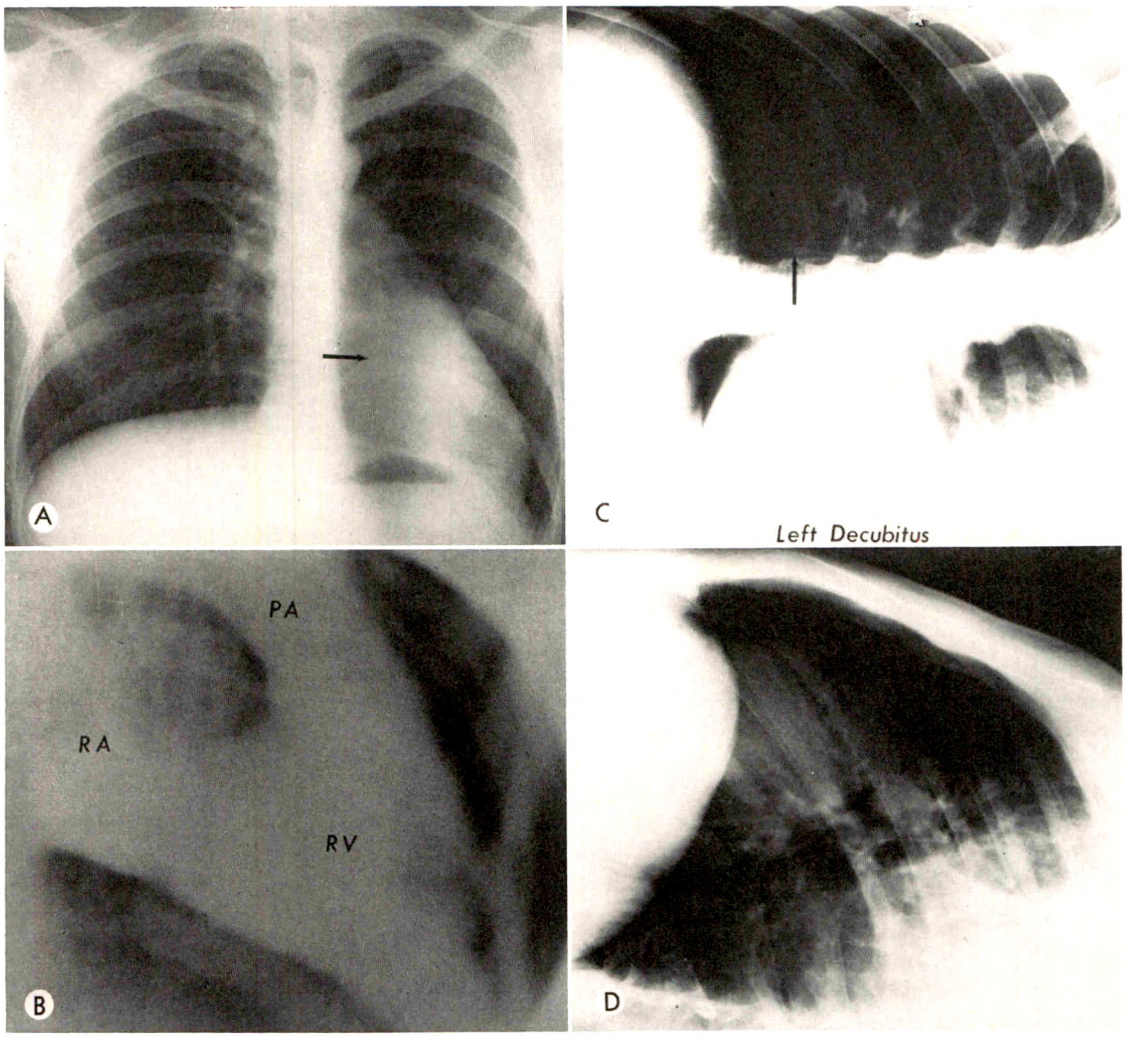


Fig. 1. (*A*) Posteroanterior conventional plain roentgenogram showing levoposition of the heart with prominence of the pulmonary artery segment. Arrow indicates vertical plane where the free edge of the pericardium was demonstrated on cinefluoroscopy. (*B*) Right ventricular anteroposterior angiocardiogram with leftward displacement of the right ventricle (RV) and pulmonary artery (PA). (*C*) Left decubitus roentgenogram demonstrating passage of air injected in left pleural space to the right pericardial sac (arrow). (*D*) Lateral supine roentgenogram demonstrating increased retrosternal space.

roentgenography. Dimond and associates,[13] in 1960, were the first to make an angiographic diagnosis of a partial left pericardial defect. Chang and Amory,[8] in 1965, reported the first angiographic diagnosis of a partial right pericardial defect.

Embryology and Classification of Defects

The exact embryologic development of pericardial defects is unknown. There is good evidence suggesting early atrophy of the left duct of Cuvier, which is responsible for the blood supply to the embryonic pleuropericardial membrane. In normal subjects, this membrane eventually forms the left pericardium. The right duct of Cuvier normally persists as the superior vena cava and thus assures adequate nutrition to the right pleuropericardial membrane.[47,48] Others have postulated that herniation of an abnormal lung bud through the pleuropericardial foramen may result in the anomaly.[41]

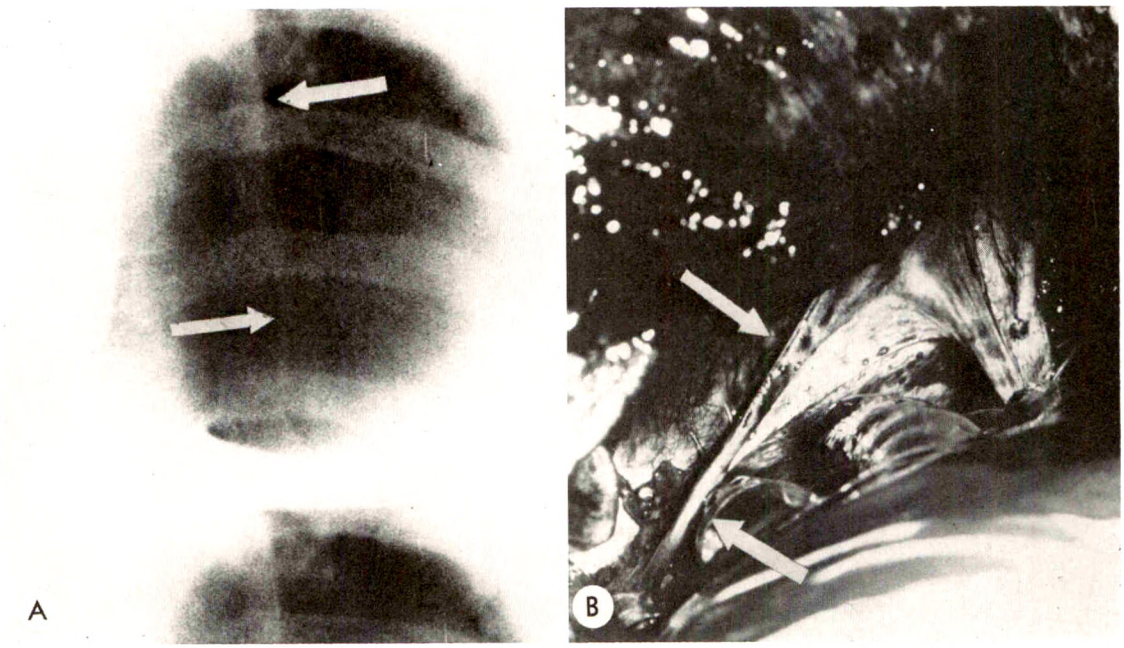


FIG. 2. (*A*) Anteroposterior enlarged 16 mm. cinefluoroscopic frame showing thickened pericardial edge indicated by arrows. (*B*) Surgical photograph. Arrows indicate free medial edge of the remaining right pericardium.

It is apparent (Table 1) that congenital absence of the left pericardium (partial and total types) accounts for the vast majority of cases. Congenital absence of the right pericardium (partial type) is rare and absence of the entire pericardium (left and right sides) as well as defects at the base of the pericardium is more infrequent.

Forty-three of the 87 cases (49 per cent) had associated pathology of the heart and lungs. There was increased incidence of bronchogenic cyst (9 cases)[24,26,34,41,53] and patent ductus arteriosus (8 cases).[4,5,7,25,29,31,45] Other less frequently associated were mitral stenosis[25,43,56] and tuberculosis[25] (3 cases in each), and pulmonary sequestration (2 cases).[21,54]

CLINICAL FEATURES

There were 47 males and 30 females. No information regarding sex was given for 10 of the patients. The mean age at the time of diagnosis was 21 years with a range from newborn to 81 years.

Reviewing the reported cases in 1938, Southworth and Stevenson[47] found only 3 cases in which the cardiovascular symptomatology was thought to be due to the pericardial defect. These included 2 cases of angina pectoris and 1 case of pericarditis.

A history of chest pain was mentioned in 17 cases including our case.[6,8,14,15,17,22,32,34,35,41,44,47,50,52,55] Nature and cause of the chest pain was presumed to be related to the pericardial defect.

Sixteen patients (including our case) had heart murmurs which could be accounted for by the pericardial defect.[3,12,15,17,18,22,37,41,42,51,52,55] Virtually all of the murmurs were systolic. While murmurs varied in location and intensity, they were usually heard along the left sternal border or in the pulmonary area.

There were 15 patients with abnormal point of maximal cardiac impulse and all of these were associated with complete absence of the left pericardium. The heart size of cases reviewed were normal except for those with associated other cardiac anomalies.

Eighteen patients including the present

TABLE I

CONGENITAL PERICARDIAL DEFECTS
87 cases from 1939 to 1967

I Partial—47						II Total—40					
Year	Author	Reference No.	Year	Author	Reference No.	Year	Author	Reference No.	Year	Author	Reference No.
A. Left—40						A. Left—37					
1941	Osgood	36	1962	Duffie	14	1936	Ladd	30	1962	Sato	43
1944	Sunderland (A)	48	1962	Lindskog	31	1938	Southworth	47	1963	Cuccurullo	10
1945	Rusby	41	1962	Parmley	37	1939	Kadin (A)	27	1963	Inada (C)	25
1953	Fry	19	1962	Voronov	53	1944	Ronka	40	1964	Fisher (A)	17
1955	Jones (A)	26	1963	Horiide	24	1944	Sunderland (B)	48	1964	Fisher (B)	17
1955	Jones (B)	26	1963	Inada (A)	25	1951	Shafiroff	46	1964	Wolf	56
1955	Jones (C)	26	1963	Inada (B)	25	1952	Matsukura	25	1965	Dimich	12
1958	Horiuchi	25	1963	Tucker (A)	52	1956	Fuke	25	1965	Tabakin (A)	51
1958	Kjellberg	29	1963	Tucker (B)	52	1957	Kumano	25	1965	Tabakin (B)	51
1958	Wada	25	1963	Williams (A)	55	1957	Maganabe	25	1965	Motolese-Lazzàro	33
1960	Dimond	13	1963	Williams (B)	55	1959	Ellis (A)	15	1966	Broadbent (A)	5
1960	Hering (A)	22	1964	Hipona (B)	23	1959	Ellis (B)	15	1966	Broadbent (B)	5
1960	Hering (B)	22	1964	Mukerjee	34	1959	Takaura	25	1966	Broadbent (C)	5
1961	Bor (B)	4	1964	Swanson	50	1960	Aoki	25	1966	Broadbent (D)	5
1961	Bor (C)	4	1965	Baker	2	1960	Kamoto	25	1966	Broadbent (E)	5
1961	Chang	7	1965	Samet	42	1961	Bor (A)	4	1966	Nasser	35
1961	Kavanagh-Gray	28	1965	Schuster	45	1961	Hamilton	21	1967	Schumacher	44
1961	Suzuki (A)	49	1966	Broadbent (F)	5	1962	Boone	3	1967	Glover	
1961	Suzuki (B)	49	1966	Broadbent (G)	5	1962	Fowler	18			
1962	Bruning	6	1966	Rogge	39						
B. Right—5						B. Right—0					
1955	Jones (C)	26	1965	Chang	8	No Cases					
1955	Jones (E)	26	1966	Fusonie	20*						
1964	Hipona (A)	23									
C. Base of heart—2						C. Left and Right—3					
1939	Kadin (B)	27				1939	Kadin (C)	27			
1966	Reese	38				1953	Moore	32			
						1958	Warner	54			

* Note: 30 cases reported of associated anomalies of base of pericardium, abdominal wall, sternum and diaphragm. Letters in parentheses: cases.

case, had abnormal electrocardiograms[5,12,13,15,17,18,22,35,37,42,44,51] that could be related to the pericardial defect. In the majority of these patients, the defect was complete absence on the left side with right axis deviation.

ROENTGENOLOGIC FINDINGS

CONVENTIONAL PLAIN FILM ROENTGENOGRAMS

The roentgenographic findings depend on the size and location of the defect.

The plain film roentgenographic findings in complete absence of the left pericardium are:

1. When the defect is large or complete on the left side, the heart is displaced to the left with concomitant clockwise rotation so that the left border is formed by the right ventricle.
2. There are varying degrees of prominence of the pulmonary artery trunk along the left upper heart border.

3. Abnormal mobility of the heart might be appreciated on a roentgenogram made with the patient in a supine position and with the roentgen-ray beam directed horizontally, thereby demonstrating increased diameter of the retrosternal clear space (Fig. 1*D*).

Unlike those with complete absence of the left pericardium, the roentgenographic findings in partial or small left-sided pericardial defect is not characteristic. The heart is in normal position. The configuration of the heart, however, is abnormal, except for those cases without extension of the left atrial appendage outside the confines of the defect. The abnormality consists of varying degrees of prominence or enlargement in the vicinity of the left atrial appendage along the left upper heart border. In a given case, however, it is difficult to ascertain which produces the prominence, left atrial appendage or pulmonary artery.

Five cases with partial right-sided defects revealed an abnormal bulge along the right upper heart border in the vicinity of the superior vena cava due to protrusion of a part of the right atrium through the defect. There was 1 case,[23] however, in which a part of the right upper lobe of the lung had herniated into the pericardial sac.

No case report could be located of complete absence of the pericardium on the right side.

Roentgenographic and clinical misinterpretations have led to such tentative diagnoses as left ventricular aneurysm,[13] tumor of the lung,[44] pheochromocytoma,[37] cardiac tumor,[55] mitral valve disease,[55] atrial septal defect,[12,35] bronchogenic carcinoma,[52] mediastinal tumor,[14,28] pulmonary stenosis,[15,39] and corrected transposition of the great vessels (present case report).

FLUOROSCOPY

The fluoroscopic findings were mentioned in 22 of the cases reviewed. In total absence of the left pericardium, increased pulsations of the pulmonary artery segment were observed in 2 cases;[21,51] normal pulsations were noted in 1 case;[35] the remaining 2 cases[18,47] were considered nonspecific. It would seem, therefore, that pulsations in total absence of the left pericardium are essentially normal other than for some cases where pulsations of the main pulmonary artery trunk and/or left pulmonary artery may be increased.

In partial or small left-sided pericardial defects, paradoxical pulsation of the left upper heart protuberance was noted compared with the aorta and the pulmonary arteries.[7,45,52] The remaining 10 cases showed no such finding.[2,13,19,22,34,39,41,42]

Thus it follows that fluoroscopy is of limited value except in those cases where paradoxical pulsations may be seen.

Only 1 fluoroscopic report was located of a partial right-sided pericardial defect.[45] It described paradoxical pulsation in the right cardiac border.

In the case presented in this report, the free edge of the remaining right pericardium was demonstrated on cinefluoroscopy; this was proven at surgery. It seems doubtful that such a line could be seen with partial pericardial defects. The free edge of the pericardium was rolled and thereby produced enough density to be seen on cine film. Most reports in this review did not describe the free edge, although some[7,18,22,32,40,41] have noted it to be prominent in one way or another (Fig. 2, *A* and *B*).

ANGIOCARDIOGRAPHY

Twenty-three angiocardiographic reports were reviewed,[2,8,12,13,14,15,18,22,23,28,32,39,42,45,50,51,52,55] including the present case.

Angiocardiography in complete or large left-sided defects is usually not necessary because of the rather characteristic conventional plain film roentgen findings. Nevertheless, such a study will reveal that not only is the heart displaced to the left but also there is some clockwise rotation of the heart whereby the left heart border is formed by the right ventricle; also, the main pulmonary artery trunk

forms the left upper heart border beneath the aorta.

All evidence indicates that angiocardiography is invaluable in the diagnosis of left or right-sided partial defects to exclude a mediastinal mass or anomaly of the pulmonary artery. Of the 40 cases of partial left-sided defect, 29 had herniation of the left atrial appendage and 11 did not.[4,5,24,25,26,28,29,31]

PNEUMOTHORAX

A total of 14 cases had diagnostic pneumothorax. Of these cases, 2, plus our cases, had angiocardiography, pneumothorax, and surgery;[2,51] 4 had angiocardiography and pneumothorax studies only;[3,12,18,39] 3 had pneumothorax study and surgery only;[15,41,51] and 4 had pneumothorax studies without angiocardiography or surgery.[5,15,17,35] It is interesting to note that the pneumothorax studies described were all done in total absence of the left pericardium except for 3[2,39,41] with partial left pericardial defects.

The demonstration of pneumopericardium after the induction of the pneumothorax may be regarded as diagnostic of congenital pericardial deficiency. The usual technique in adults consists of introducing 400–500 cc. of air into the left pleural space. With a horizontal beam, filming is carried out in the anteroposterior and lateral projections with the patient supine and in the lateral decubitus position. For examination in the left lateral decubitus position, one roentgenogram should be made with the patient in the straight decubitus position and another with a slight right posterior oblique position in relation to the film.

A normal pneumothorax study does not exclude the diagnosis of pericardial defect because: (a) Air introduced into the pleural space will have free access to the pericardial pleural space only if there is a defect in the parietal pleura in addition to the pericardial defect. The percentage of cases with or without associated defects of parietal pleura is unknown, although Southworth and Stevenson,[47] in 1938, stated that 76 per cent of cases had a common pleuropericardial cavity on the left and that 24 per cent had only a pleuropericardial foramen. (b) For reasons not entirely clear, numerous roentgenograms may, on occasion, be necessary to demonstrate the transgression of air to the pericardial space. (c) It seems theoretically possible that in cases with adjacent pulmonary pathology overlying the defect or with small defects, a pneumothorax study might not be diagnostic.

SURGICAL TREATMENT

Of the 87 cases reviewed, 53 had surgery. There is no consistent surgical treatment of choice for repair of pericardial defects. No surgical treatment for complete absence of the left pericardium would seem to be indicated in most cases. There is one reported case,[44] however, in which a silastic graft was used to stabilize the heart.

In partial absence of the left pericardium, no surgical correction was attempted in approximately half of the cases, whereas in the remaining half, surgical procedures varied: excision of the left atrial appendage; excision or splitting of the pericardium; and closure of the defect by sutures alone or with a pleural flap.

SUMMARY

Congenital absence of the pericardium should not be considered rare. Of the 87 cases reviewed, congenital absence of the left pericardium (partial and total types) accounted for the vast majority of cases. Congenital absence of the right pericardium (partial and total types) is relatively unusual and absence of the entire pericardium (left and right sides) as well as defects at the base of the pericardium are rare.

The appearance of complete absence of the left pericardium as seen with conventional plain film roentgenography is characteristic. The presence of right axis deviation on the electrocardiogram, a systolic precordial murmur, as well as displacement of the point of maximal cardiac im-

pulse may be present in various combinations.

The appearance of partial left or partial right pericardial defects as seen with conventional plain film roentgenography is not characteristic and requires a high index of suspicion for diagnosis. Angiocardiography is the method of choice for diagnosis.

Cinefluoroscopic demonstration of the free rolled edge of the remaining pericardium is presented.

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CALCIFICATION OF THE TRICUSPID ANNULUS*

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ALTHOUGH calcific deposits are frequently found in the left heart valves and valve rings, they are rarely seen in the right heart. Only 2 cases of calcific pulmonary valve stenosis were reported in the radiologic literature[6] prior to the report by Dinsmore *et al.*[2] in 1966 of 5 cases of congenital valvular pulmonary stenosis with calcification. More recently, 7 additional cases, 5 of which were demonstrated roentgenographically, have been reported.[8] Tricuspid valvular calcification is even more rarely observed,[8,11] and only isolated case reports are on record.[1,3,9,10] These have been associated with ventricular septal defect,[9,10] rheumatic heart disease,[3] congenital malformation of the tricuspid valve,[10] and possibly subacute bacterial endocarditis.[8] No case of tricuspid annular calcification comparable to the mitral annular calcification frequently observed in the aged can be found in the English language literature.

We have observed 4 cases with roentgenographic findings suggesting calcification of the tricuspid annulus (Table 1). In all cases there was a background of prolonged elevated right ventricular pressure. Three patients had congenital valvular pulmonary stenosis (2 exhibited calcification in the pulmonary valve), and 1 patient had an atrial septal defect with pulmonary arterial hypertension.

REPORT OF CASES

CASE 1. B. T., a 51 year old female was admitted to Emory University Hospital because of recent atrial fibrillation. She gave a history of dyspnea and mild chest pain of 5 months' duration. There was no history of rheumatic fever. Physical examination revealed a blood pressure of 150/80 and a regular pulse of 80. Her heart was moderately enlarged and a Grade 4 ejection systolic murmur was present along the left sternal border which radiated to the neck and back. Electrocardiography showed right axis deviation and the phonocardiogram confirmed fixed wide splitting of the second sound with diminished pulmonic component. Fluoroscopy and roentgenography revealed increased amplitude of pulsation of the main pulmonary artery and left branch, moderate calcification of the pulmonary value, extensive calcification of the tricuspid annulus (Fig. 1, *A* and *B*), and moderate cardiac enlargement with right ventricular predominance.

At cardiac catheterization an atrial septal defect with a small left-to-right shunt was demonstrated. There was moderate elevation of the right ventricular pressure (65/9 mm. Hg) with a 33 mm. Hg gradient across the pulmonary valve. Cineangiography confirmed the localization of the intracardiac calcifications to the pulmonary valve and tricuspid annulus. There was no gradient across the tricuspid valve.

CASE II. R. W., a 42 year old male was found to have had a heart murmur in early childhood with no history of rheumatic fever. Since age 21 he experienced intermittent dyspnea and chest pain and had at least one illness due to pulmonary embolus. Physical examination revealed a Grade 3 precordial systolic ejection murmur. Chest roentgenography revealed a markedly enlarged heart and main pulmonary artery, and calcification in the tricuspid region (Fig. 2, *A* and *B*).

Cardiac catheterization was performed which revealed an atrial septal defect with a large left-to-right shunt (2.8 to 1). There was moderate pulmonary arterial (70/25 mm. Hg) and right ventricular hypertension, but no gradient

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Table I

SUMMARY OF CASES

	Age	Sex	Underlying Lesion	Rheumatic Fever or Subacute Bacterial Endocarditis	Catheterization Data		Calcification on Roentgenography		Clinical Course
					Tricuspid Stenosis	Right Ventricular Pressure (mm. Hg)	Tricuspid Ring	Pulmonary Valve	
Case I. B.T.	51	F	Valvular pulmonary stenosis. Atrial septal defect	o	o	69/9	++++	++	Satisfactory. Not operated
Case II. R.W.	42	M	Atrial septal defect	o	o	70/10	+	o	Repair of atrial septal defect. Calcification identified at surgery
Case III. H.S.	51	M	Valvular pulmonary stenosis	o	o	165/10	++++	o	Pulmonary valvulotomy. Improved
Case IV. V.C.	51	F	Valvular pulmonary stenosis. Probable atrial septal defect	o	—	—*	++++	++++	Died. No autopsy

* Electrocardiography showed marked right ventricular hypertrophy and right ventricular strain.

across the pulmonary valve. Cineangiography demonstrated a dense crescent of calcium in the tricuspid valve ring. There was no gradient across the tricuspid valve.

The patient underwent successful surgical repair of the atrial septal defect. At surgery calcification was confirmed in the tricuspid ring and adjacent area of the posterior leaflet of the tricuspid valve.

Case III. H. S., a 51 year old male was admitted to Emory University Hospital because of progressive dyspnea, the diagnosis of congenital pulmonary stenosis having been made in childhood. Physical examination revealed a harsh murmur of pulmonary valvular stenosis. Chest roentgenograms showed cardiac enlargement involving primarily the right ventricle. There was poststenotic dilatation of the main pulmonary artery segment. Dense calcification was identified in the tricuspid annulus on roentgenography and fluoroscopy (Fig. 3, *A* and *B*).

Cardiac catheterization was performed and showed a markedly elevated right ventricular pressure with a large gradient across the pulmonic valve. There was no gradient across the tricuspid valve.

The patient underwent a pulmonary valvulotomy with moderate improvement in his symptoms.

Case IV. V. C., a 51 year old female entered Emory University Hospital because of progressive dyspnea since childhood. There was a history of murmur since infancy. She appeared chronically ill and was cyanotic. There was a loud systolic murmur heard over the entire pre-

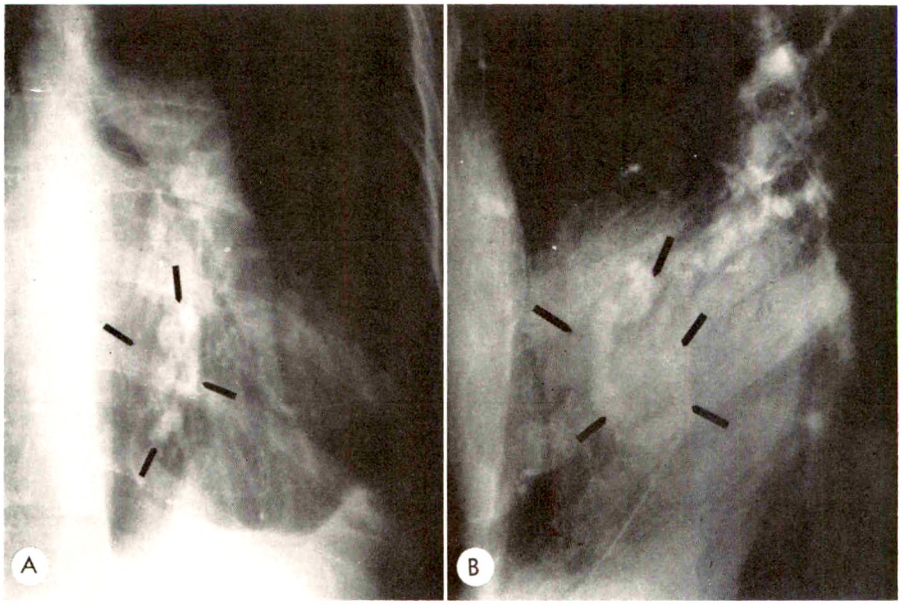


FIG. 1. Case I. (*A*) Posteroanterior roentgenogram. Note similarity of calcified tricuspid annulus to the mitral annulus in this position. This patient also had a calcified pulmonary valve demonstrated on cinefluorography. (*B*) Left lateral roentgenogram. The calcified tricuspid ring is located in the anterior third of the cardiac shadow and is incompletely calcified centrally adjacent to the aortic root. This produces a "C" configuration.

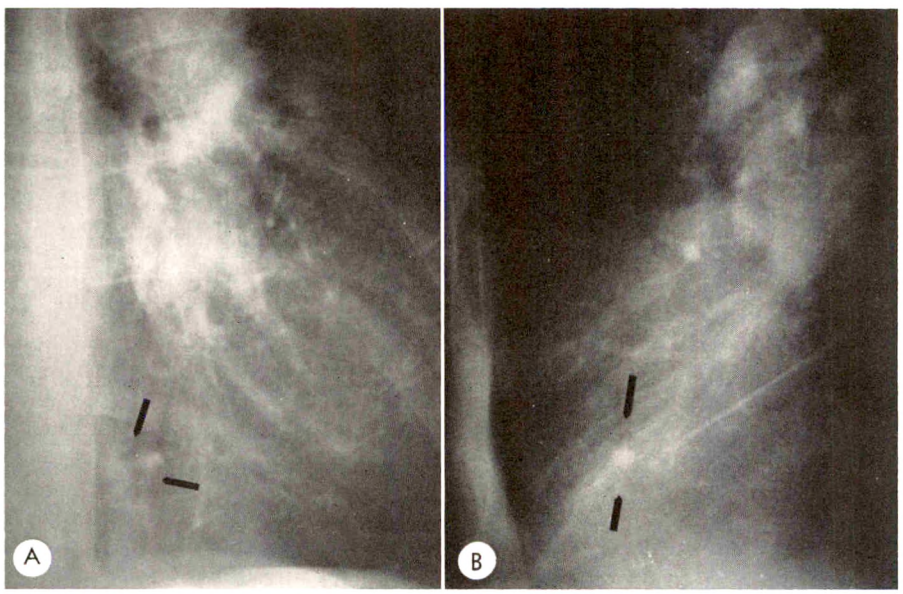


FIG. 2. Case II. (*A*) Posteroanterior roentgenogram. A small crescent of calcification is demonstrated in the tricuspid area. This was localized to the annulus and adjacent area of the posterior leaflet of the tricuspid valve at surgery and on cineangiography. (*B*) Left lateral roentgenogram. The calcification is confined to a small area in the anterior third of the cardiac shadow.

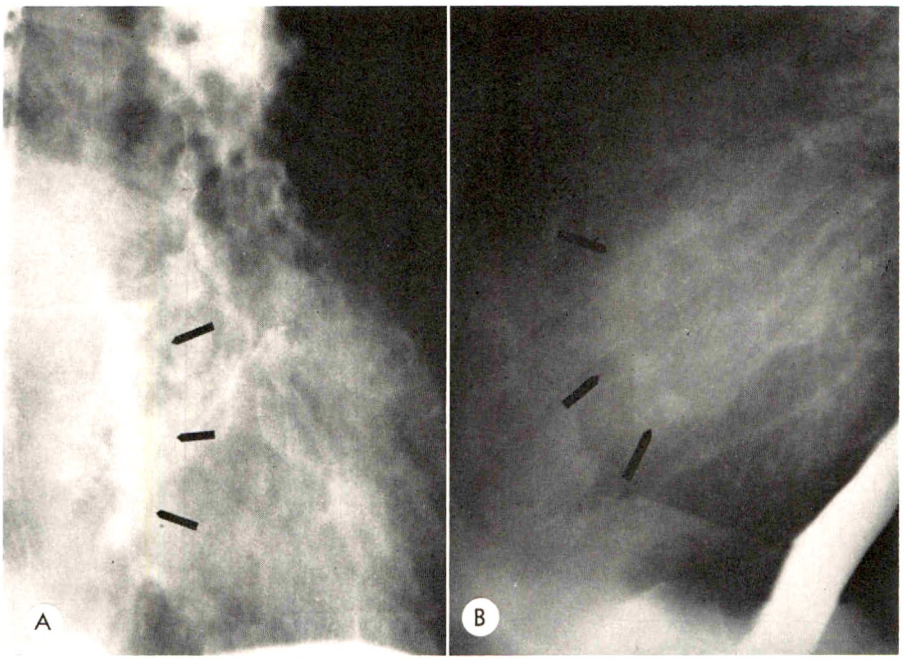


Fig. 3. Case III. (*A*) Posteroanterior roentgenogram. The annular calcification was observed fluoroscopically and simulated a calcified mitral ring in this position. (*B*) Left lateral roentgenogram. The anterior location and "C" configuration localize the calcification to the tricuspid annulus in this patient with congenital valvular pulmonary stenosis.

cordium. Electrocardiography showed right ventricular hypertrophy and strain. Chest roentgenography and fluoroscopy revealed marked cardiac enlargement with pulmonary edema. There was dense calcification in the pulmonary valve and, in addition, a dense ring of calcium in the tricuspid annulus (Fig. 4).

The diagnosis of valvular pulmonary stenosis with congenital intracardiac right-to-left shunt was made clinically. The patient was considered too ill to tolerate cardiac surgery. She expired shortly after admission and no autopsy was obtained.

DISCUSSION

The striking enhancement of the fluoroscopic display with the image intensifier has made identification of intracardiac calcifications commonplace. These calcifications

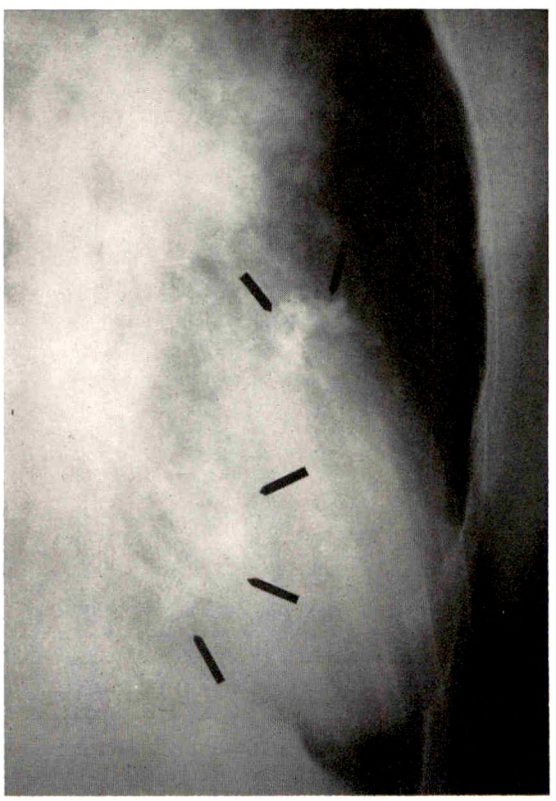


Fig. 4. Case IV. Right anterior oblique roentgenogram. Marked calcification of pulmonary valve and tricuspid annulus in a patient who died shortly after admission to the hospital. No autopsy could be obtained.

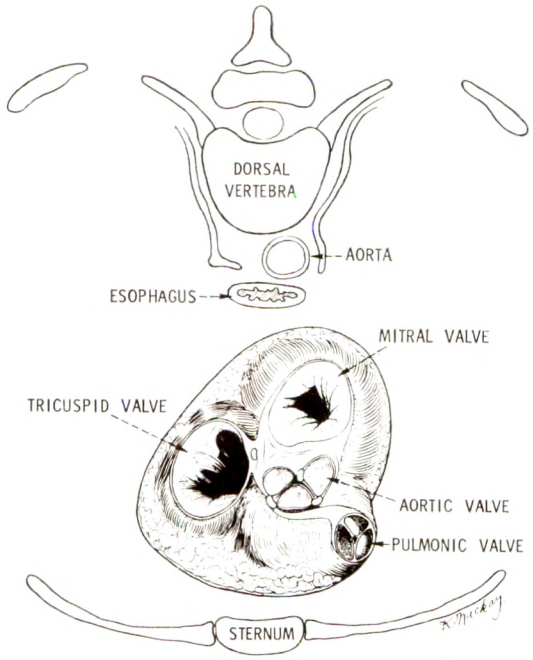


FIG. 5. Artist's drawing of base of heart with atria removed exposing the valves and valve rings. The valve plane is slightly tilted. The aortic annulus is in the center. The tricuspid valve ring is toward the right and extends anterior to the aortic valve. The mitral annulus is posterior and extends to the left of the aortic valve. The pulmonary valve is anterior and to the left.

are easily recorded in multiple projections by cinefluorography, and precise anatomic localization is usually possible *in vivo*.

In Figure 5, the anteroposterior and mediolateral relationships of the various valve rings are depicted by a medical illustrator. Figure 6, *A* and *B* demonstrates the usual position of the valve rings in posteroanterior and left lateral roentgenograms of the chest. Although the tricuspid valve ring is somewhat inferior and to the right of the mitral annulus, the partial superimposition of these rings leads to difficulty in differentiation when one ring is calcified and demonstrated only in the frontal projection. However, when viewed in the left anterior oblique or left lateral projection, these rings can be readily differentiated since the tricuspid ring is located in the anterior third of the cardiac shadow and the mitral annulus in the posterior third (Fig. 7, *A* and *B*).

Although, on occasion, the entire mitral annulus may be calcified, it is uncommon for the central portion adjacent to the aortic root formed by the fibrous trigones to contain gross calcification. This pro-

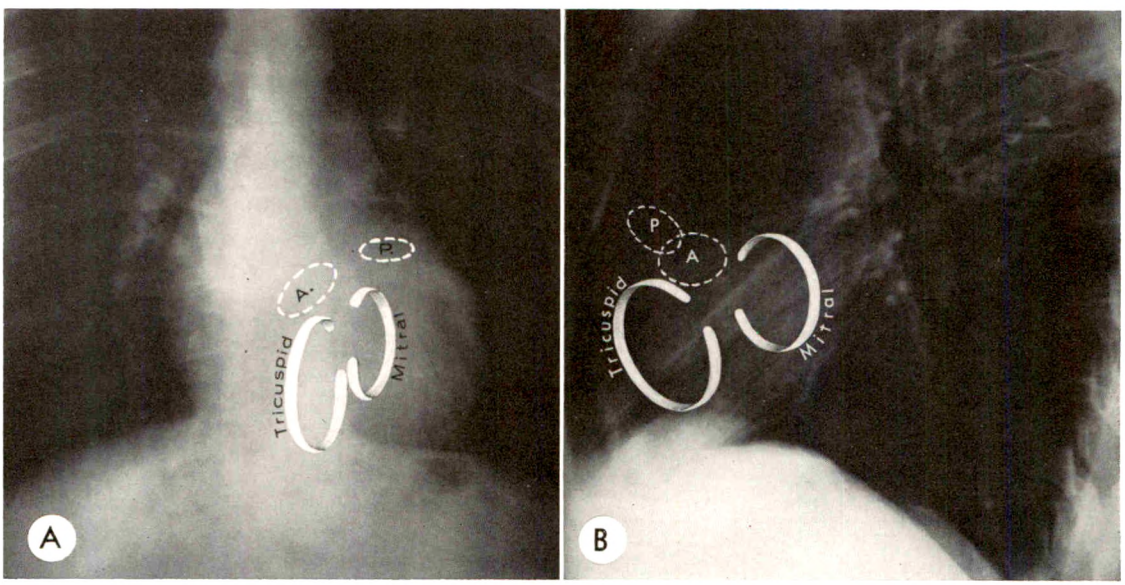


FIG. 6. (*A*) Relative position of the valve rings indicated on a posteroanterior roentgenogram. Only the portions of the mitral and tricuspid rings that usually calcify are demonstrated. (*B*) Relative position of the valve rings in the left lateral projection. Note the "C" appearance of the calcified portion of the tricuspid annulus and the mirror image, "reverse C" appearance of the mitral annulus.

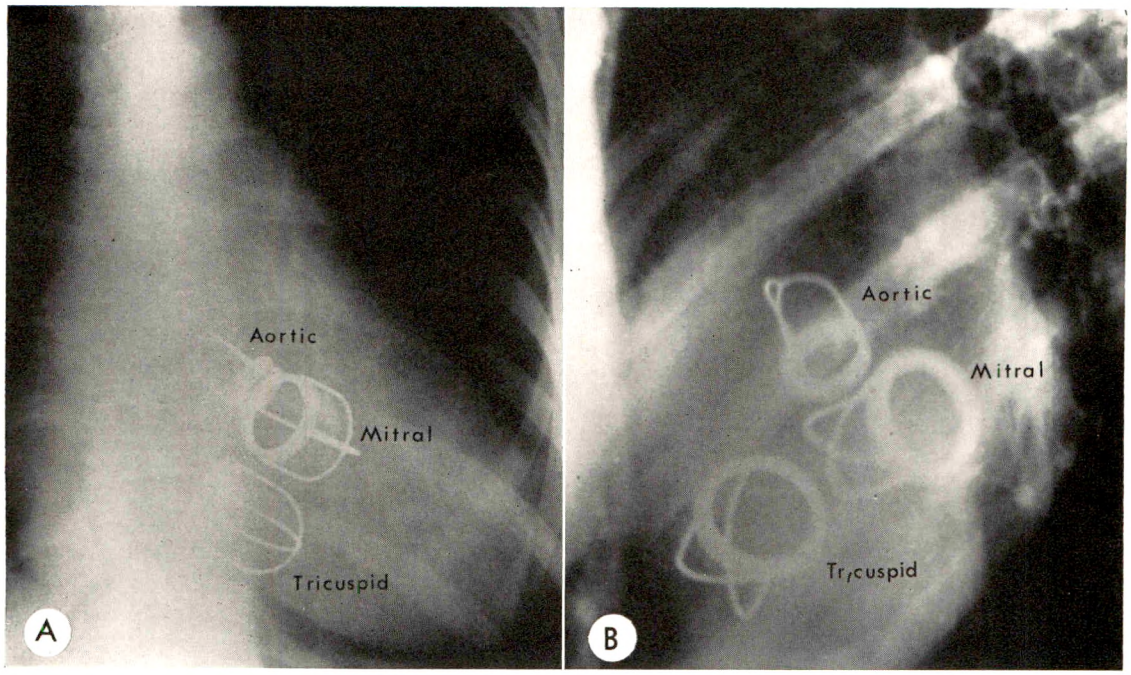


Fig. 7. (*A*) Posteroanterior roentgenogram showing prosthetic tricuspid, mitral and aortic valves in a postoperative patient. (*B*) Left lateral roentgenogram of the same patient.

duces a "reverse C" configuration when viewed in the left anterior oblique or left lateral projection (Fig. 8, *A* and *B*). The tricuspid annulus by contrast produces almost a mirror image of the mitral annulus, since the central portion of this ring formed by the right fibrous trigone is not calcified in any of our cases. This produces a "C" configuration in the left lateral or left anterior oblique projection.

Calcification of the mitral annulus is generally considered to be a degenerative change related to the aging process and relatively unimportant clinically. It is found most frequently in elderly females and may be associated with a soft apical systolic murmur. Rarely is the process of sufficient magnitude to produce hemodynamically significant mitral stenosis or insufficiency.[5] On occasion it may extend to involve the fibrous trigones and septum membranaceum to the extent that heart block results from impairment of the conduction system.[12]

The annuli or valve rings form the fibrous cardiac skeleton. To these the atrial and ventricular myocardial bundles attach and from these the valve leaflets are hung. In the infant the annuli are composed of fibrillar, parallel collagen bundles separated by a clear ground substance. Serial pathologic studies of the mitral annulus show that the collagen gradually undergoes changes in the child and young adult, the fibers becoming swollen and losing their parallel arrangement. Lipid deposits occur in the third decade, and, about 45 years of age, foci of calcification are demonstrable in these areas. Histologic studies of cases of massive mitral annulus calcification suggest that these lesions represent an exaggeration of the above "aging" process.[5]

Since the composition and function of the mitral and tricuspid annuli are similar, it seems justifiable to assume that the more frequent calcification of the mitral annulus is related to the higher pressure in the left ventricle. If long-standing elevation of the right ventricular pressure is present, as in the cases presented here, one may speculate that the aging of the tricuspid annulus is accelerated, and that in some cases de-

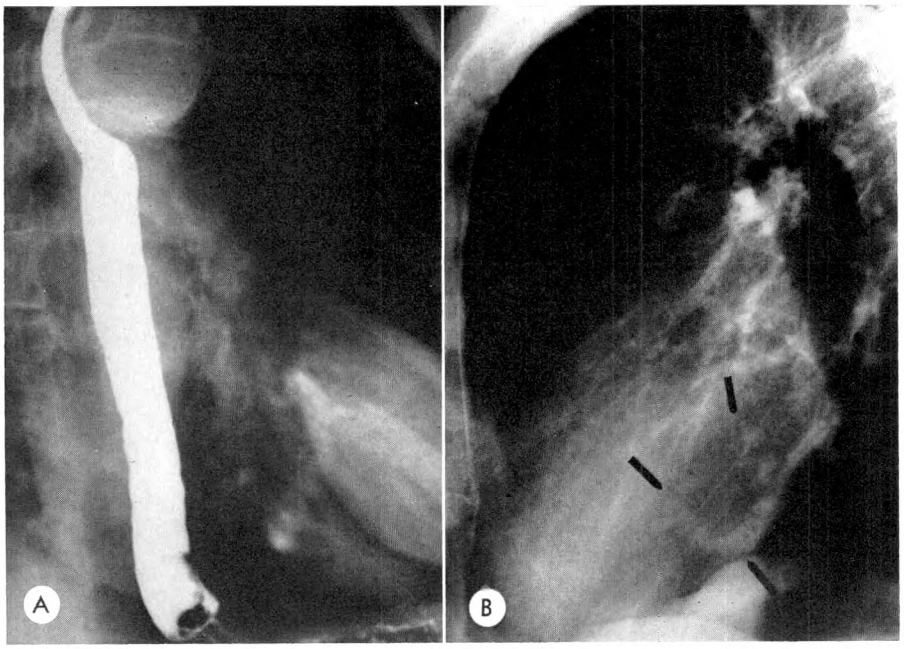


FIG. 8. (*A*) Posteroanterior roentgenogram. Calcified mitral annulus. (*B*) Left lateral roentgenogram. Calcified mitral annulus. Note localization to posterior third of the cardiac shadow with incomplete calcification of the ring centrally, producing a "reverse C" configuration.

generative calcification occurs.

We have found no other reports of calcification of the tricuspid ring, which was roentgenologically visible, in the English language literature. There is one report from Russia of a patient with severe arteriosclerosis and pulmonary emphysema with probable cor pulmonale who was shown to have tricuspid annulus calcification demonstrated by tomography.[7] Another case is reported from Italy of an autopsy on an elderly patient with severe stenosis of the pulmonary valve in which there was dense calcium in the tricuspid annulus.[4] These cases are similar to our own in that there was prolonged elevation of the right ventricular pressure. This reinforces our impression that calcification of the tricuspid annulus, like that of the mitral, is basically a degenerative process and may be accelerated by increased right ventricular pressure.

SUMMARY

Four cases with tricuspid annular calcification, identified roentgenographically, are reported.

The increased stress on the tricuspid ring from prolonged increase in right ventricular pressure is believed to be a significant factor in all of these cases.

The appearance of the calcified annulus and the method of roentgenologic localization are described.

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PULMONARY ARTERIOGRAPHY: A SIMPLE METHOD FOR DEMONSTRATION OF CLINICALLY SIGNIFICANT PULMONARY EMBOLI*

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THE absence of specific symptoms makes the clinical diagnosis of a minor pulmonary embolus almost impossible.[1] Even larger pulmonary emboli are often difficult to diagnose clinically, and frequently cannot be differentiated from myocardial infarction, pneumonia, cholecystitis, or subdiaphragmatic abscess. The choice of proper treatment, however, makes a differential diagnosis important, and the radiologist is frequently asked to help the clinician make his decision.

A pulmonary embolus may show a variety of manifestations on a chest roentgenogram. The lungs may appear completely normal without pleural effusion or elevation of the diaphragms—even after massive occlusion of a large branch of the pulmonary artery. Sometimes, however, decreased vascularity can be noted, although a decrease can be recognized only when it is relatively far advanced. Massive occlusion may produce dilatation of the main pulmonary artery and its major branches proximal to the occlusion. Areas of plate atelectasis in both lung bases are not pathognomonic for a pulmonary embolus, but in some cases have been the only sign of an embolization. A pulmonary parenchymal infiltrate in embolization is not necessarily indicative of a pulmonary infarction, since hemorrhage into the alveoli secondary to venous backflow can produce the same appearance. In any larger embolus the pleura is involved, frequently resulting in a pleural effusion. It has been estimated that chest roentgenograms are abnormal in only 20 per cent of all cases of pulmonary emboli,[19] so that a chest roentgenogram, although occasionally suggestive of an embolus, is not a reliable test to screen for pulmonary emboli.

Two special roentgenologic techniques, lung scanning and pulmonary arteriography, have been used in the investigation for pulmonary emboli. To obtain a lung scan either macroaggregated I^{131} albumin, macroaggregated technetium 99m albumin, or indium 113m-zirconium complex can be injected intravenously. These isotopes are retained in the pulmonary vascular bed so that scanning can be performed. The intravenous injection of the isotope makes this a convenient technique, and it can be used as a screening technique in chronically ill patients with normal chest roentgenograms.[6] Scanning, however, has certain disadvantages: preparation of the latter 2 isotopes takes some time; an acutely ill patient may be difficult to immobilize for even 5 minutes; occlusion of the pulmonary vascular bed by macroaggregates is occasionally a hazard, especially in a patient with borderline pulmonary circulation after massive embolization. However, the most serious disadvantage of pulmonary scanning is that it is impossible to differentiate true pulmonary emboli from pulmonary parenchymal infiltrates resulting from masses, atelectasis, inflammatory processes, hemorrhages and pleural effusion. Decreased isotope uptake may also occur when there are no infiltrates, as a result of asthma or emphysema.[13]

No special preparation of the patient or the contrast material is needed for pulmonary arteriography and the examination can be completed within 1 hour after it has first been requested. Since about the same length of time is usually required to

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prepare the operating room for embolectomy, no time is lost in doing this procedure. The equipment consists of a frontal serial film changer, a fluoroscopic unit and an electrocardiographic monitor. A selective pulmonary arteriogram has several advantages: the bolus of injected contrast material is concentrated, giving a detailed picture of the pulmonary tree; no structures filled with contrast material, such as the right atrium, are superimposed on the pulmonary arteries; and if necessary, a superselective injection can be performed to demonstrate a branch of the pulmonary artery. Pressure measurements can be performed in the pulmonary artery and the catheter can be left in place for follow-up arteriographies, pressure measurements, and for injection of fibrinolysin if desired.

We believe that this is an uncomplicated procedure, and disagree with those who suggest that the introduction of a catheter into the main pulmonary artery does not lend itself to an emergency situation.[2] Only some practice and no surgical skill is required to introduce the catheter selectively into the pulmonary artery, and the procedure can be performed by a radiologist in a properly equipped x-ray department. There is no evidence from our series that the catheter ever dislodged thrombi from any peripheral vein or from the right heart.[17,21] Furthermore, intravenous angiography, or injection of contrast material into the right atrium with consequent dilution of the contrast material, gives a significantly less detailed picture of the pulmonary vascular tree.



Fig. 1. Gray Ödman-Kifa catheter shaped for percutaneous introduction from the femoral vein into the pulmonary artery.

METHOD

For the procedure we introduce a specially shaped gray Ödman catheter (Fig. 1) into the femoral vein using the Seldinger technique instead of a more time-consuming cutdown. The catheter is then placed into the main pulmonary artery under fluoroscopic control. When the catheter passes through the tricuspid valve or right ventricular outflow tract, temporary arrhythmia may occur, and the heart is therefore monitored by electrocardiography. After pressure measurements have been taken in the pulmonary artery, contrast material is injected, preferably with a pressure injector, and supine serial roentgenograms are taken. Maximum detail is obtained with a roentgen-ray tube with a small focal spot and short exposure time.[18] The patient is permitted to breathe even during the contrast material injection and needs to be immobilized only during the

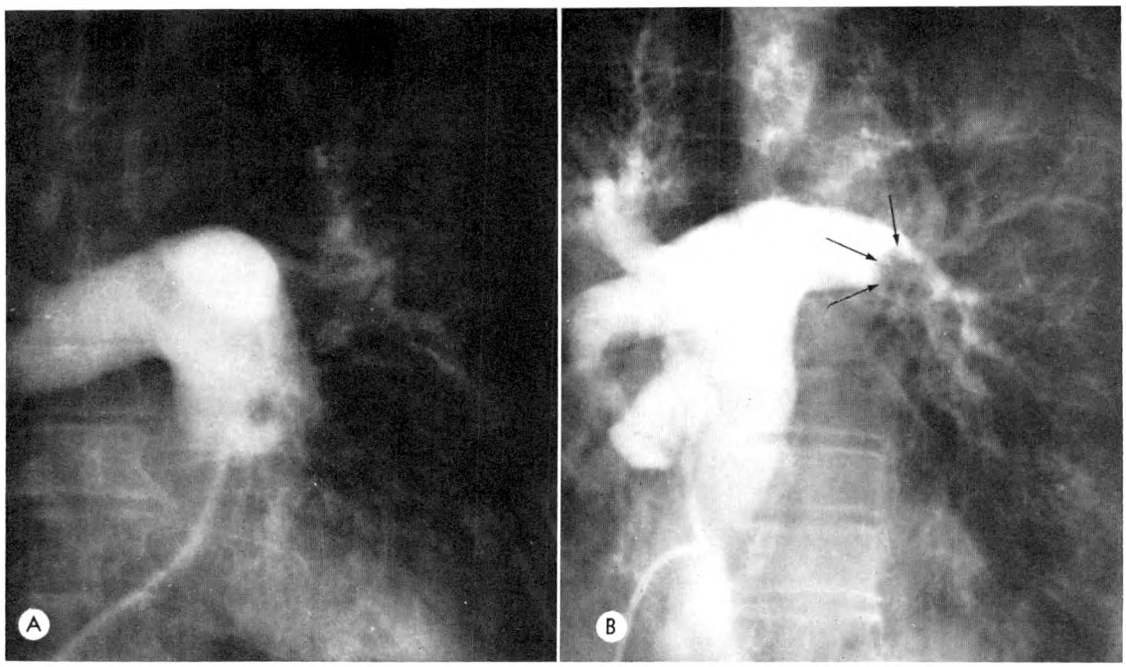


Fig 2. (*A*) Pulmonary arteriogram in supine position. The left main pulmonary artery is obscured. Decreased vascularity in periphery suggests an occlusion. (*B*) Repeat arteriogram in same patient in left anterior oblique position. A large thrombus is demonstrated in left main pulmonary artery (arrows).

approximately 30 seconds of serial filming. Occasionally it is necessary to take oblique in addition to supine roentgenograms, especially if there is a question of a lesion in the left main pulmonary artery or its lower branches (Fig. 2, *A* and *B*). Sometimes a superselective injection into one of the branches of the pulmonary artery is helpful to determine whether distal pulmonary emboli are present. There are a variety of reasons why the catheter cannot, occasionally, be introduced into the pulmonary artery. Marked irritability of the right ventricle is perhaps the most frequent reason. In these cases contrast material is injected into the right atrium.

DISCUSSION

In about 5 per cent of all patients with pulmonary emboli, the embolus is lodged in the main pulmonary artery or the right or left pulmonary artery. The classical angiographic signs of pulmonary embolus (intraluminal mass and abrupt occlusion of the pulmonary artery) are present in these cases (Fig. 3). In 10–50 per cent, the embolus has occluded one of the segmental branches, and again an intraluminal mass and abrupt vascular filling defect may be

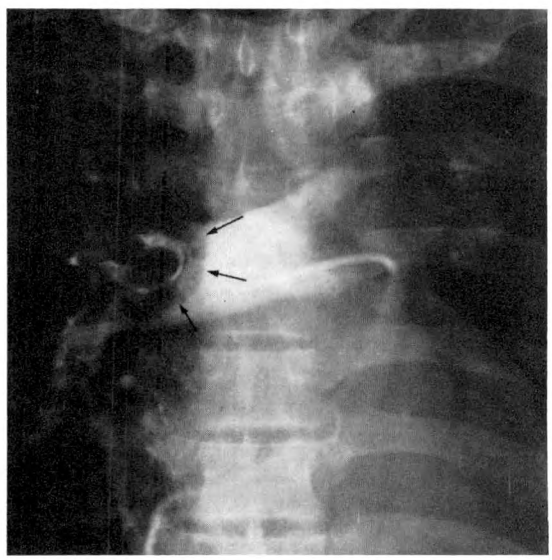


Fig. 3. Selective right pulmonary arteriogram shows saddle embolus (arrows) at the bifurcation of the right pulmonary artery.

seen on the angiogram (Fig. 4). Sometimes, however, these two criteria are difficult to find, and then indirect signs, such as peripheral oligemia, nonvisualization of the peripheral vessels, arterial stasis, and late and incomplete venous filling may help to make the diagnosis of pulmonary embolus (Fig. 5). Occlusion of small lobular branches accounts for the remainder of the cases of pulmonary emboli. An arteriogram is often negative in these instances, while occasionally an isotope scan can suggest the diagnosis of peripheral emboli. Ordinarily, the clinician is less concerned about the differential diagnosis of these peripheral emboli than he is about the more massive embolization of the first 2 groups, and the value of arteriography is that a correct diagnosis of emboli in the main pulmonary arteries or their segmental branches can be made. In such cases the arteriographic diagnosis has a high degree of accuracy.

SUMMARY

Between July 1965 and July 1968, we performed pulmonary arteriography with the technique described in 241 patients in whom the question of pulmonary emboli was raised clinically. In 65 patients the diagnosis of pulmonary embolus was confirmed angiographically, and most of these had emboli in the main pulmonary arteries or their segmental branches. Many had elevated pulmonary artery pressure, decreased peripheral arterial pressure, and a few patients had had several episodes of cardiac arrest prior to the pulmonary arteriography. Even in the group with normal pulmonary arteriograms, many patients were acutely ill and a number of them were later proven to have myocardial infarction. Despite the unfavorable condition of many patients, our complication rate is low (Table 1).

We believe that selective pulmonary arteriography using the Seldinger technique is the method of choice for the diagnosis of acute massive pulmonary emboli. It can be completed rapidly, does not

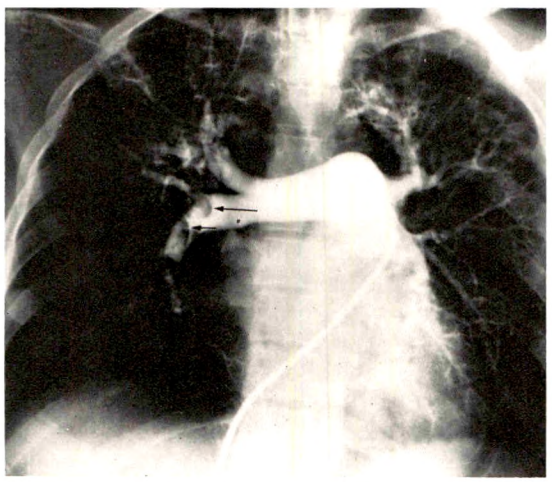


FIG. 4. Several emboli (arrows) have occluded the right lower lobe artery. Oligemia is noted in the right lower lobe.

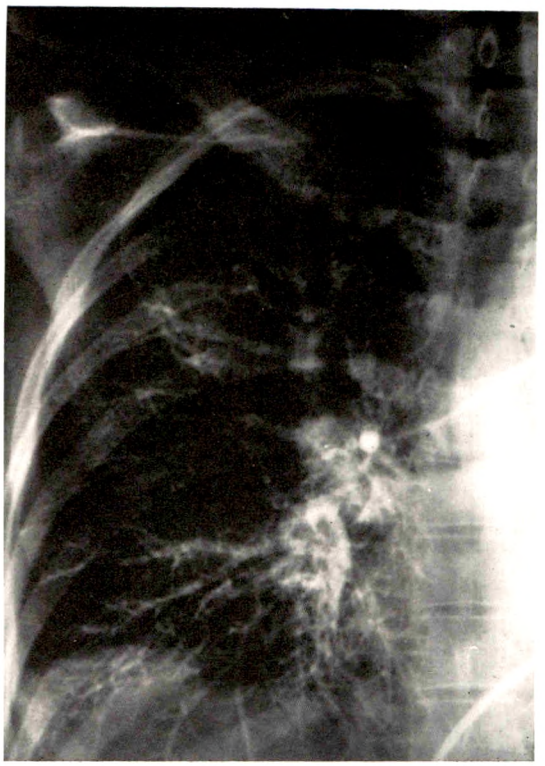


FIG. 5. Late phase of selective right pulmonary arteriogram. Venous filling is present in the upper and middle lobe, while the contrast medium is retained in many arterial branches of the right lower lobe. The many small masses and irregularities of these vessels are caused by multiple small emboli.

TABLE I

COMPLICATIONS IN 241 PULMONARY ARTERIOGRAMS

Fatal	0
Cardiac arrest	2
Partial injection into pericardium	2
Partial injection into myocardium	3
Reversible heartblock	1
Hematoma at puncture site	17

present any significant hazard even to the severely ill patient, and can be performed in the angiographic laboratory of any x-ray department.

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ROENTGENOGRAPHIC APPEARANCE OF THE TRANSPLANTED PRIMATE LUNG*

THE AUTOTRANSPLANTED LUNG

By S. H. TSAI, M.D.,† ORN ARNAR, M.D.,‡ *and* JOHN J. HAGLIN, M.D., Ph.D.‡
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TWO groups of Kenya baboons were subjected to autotransplantation (reimplantation) of the left lung at the Minneapolis Medical Research Foundation. In the first group of 26 animals,[7] the lung was extirpated after injection of heparin into the pulmonary artery. It was reimplanted immediately following perfusion with cooled low molecular weight dextran in saline. In the second group of 30 animals,[1] the lung was harvested without the use of heparin and kept at room temperature for a period of 1–3 hours before it was perfused with low molecular dextran solution and then reimplanted. There were 11 operative deaths in the first group, and 10 deaths in the second group.

Adequate roentgenographic material was furnished by the second group and formed the basis of the present study. Preoperative and postoperative chest roentgenograms of all but 4 of the baboons were available for review. All roentgenograms were made in frontal and lateral projections. The postoperative roentgenograms were taken at weekly intervals beginning on the seventh day. In addition, bronchography was done preoperatively on all animals, and postoperatively on 13 of the survivors.

OPERATIVE TECHNIQUE

The left pulmonary artery was clamped and divided. The left main bronchus was transected at a level 5 mm. proximal to the origin of the upper lobe bronchus. A cuff on the left atrium, including the ostia of the left pulmonary veins, was excised. The extirpated lung was wrapped in a moist sponge and left in a basin at room temperature for a period of 1–3 hours before it was perfused through the pulmonary artery with 500 ml. of low molecular weight dextran in physiologic saline at 4° C. It was then reimplanted by suture anastomosis of the left atrium, the pulmonary artery, and the bronchus.

ROENTGEN FINDINGS

In animals that survived the immediate postoperative period, the roentgenograms on the seventh day showed a diffuse cloudiness throughout the reimplanted lung (Fig. 1, *A* and *B*). This was an alveolar process and was associated with an air bronchogram. It varied in intensity and uniformity, and, in the great majority of cases, cleared by the end of the fourth to sixth week. Its course did not appear to have been influenced by the length of ischemia time, *i.e.*, the interval between harvesting and reimplantation of the lung.

The lung was completely atelectatic in 3 animals with complicating pneumothorax. Atelectasis of only the upper lobe was noted in 1 case with pneumothorax and in 2 cases with bronchostenosis (Fig. 2*B*).

Pneumothorax was the most frequent complication (14 out of 30 cases or 46.7 per cent). It was left-sided in 7, right-sided in 2, and bilateral in 5 instances. Unless massive, the lung, as a rule, re-expanded within 4–6 weeks without the use of chest tubes. Four deaths were associated with this complication.

A small to moderate amount of pleural fluid was usually present on the left side

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This investigation was supported by the James Picker Foundation on recommendation of the Committee on Radiology, National Academy of Sciences—National Research Council.
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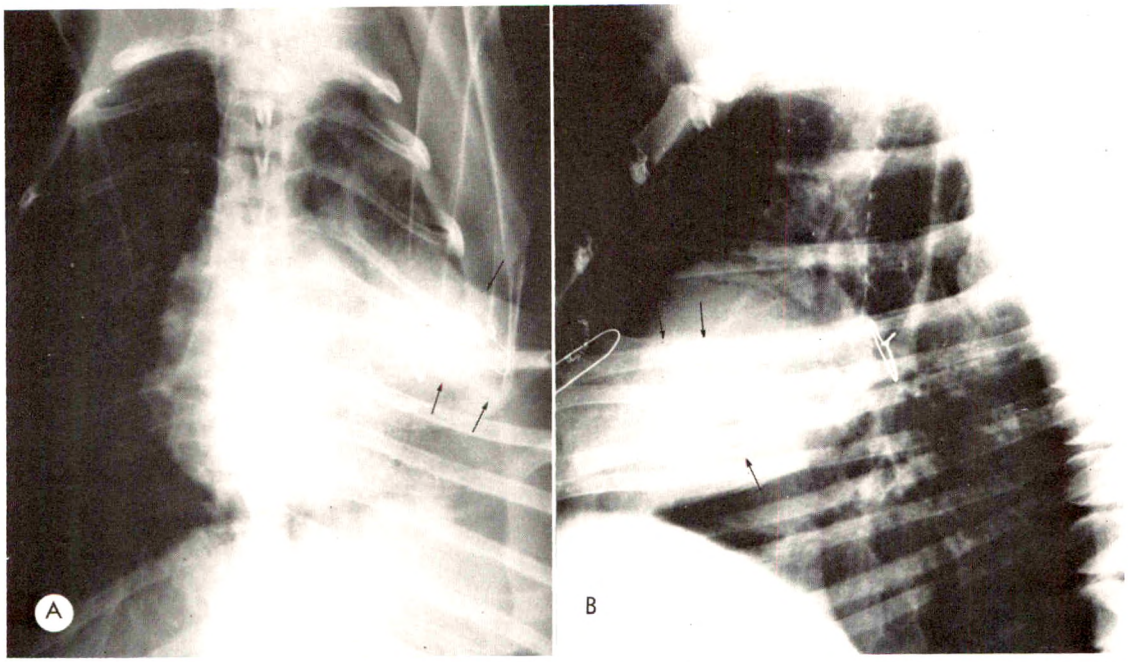


FIG. 1. Baboon No. 1005. (*A*) Frontal and (*B*) lateral roentgenograms at end of the first postoperative week. There is diffuse cloudiness of the entire left lung except its extreme apex. Note air bronchogram of the upper and lower lobes in *A*, and of the anterior segment and the lower lobe in *B*. Arrows indicate marked soft tissue reaction along the incision.

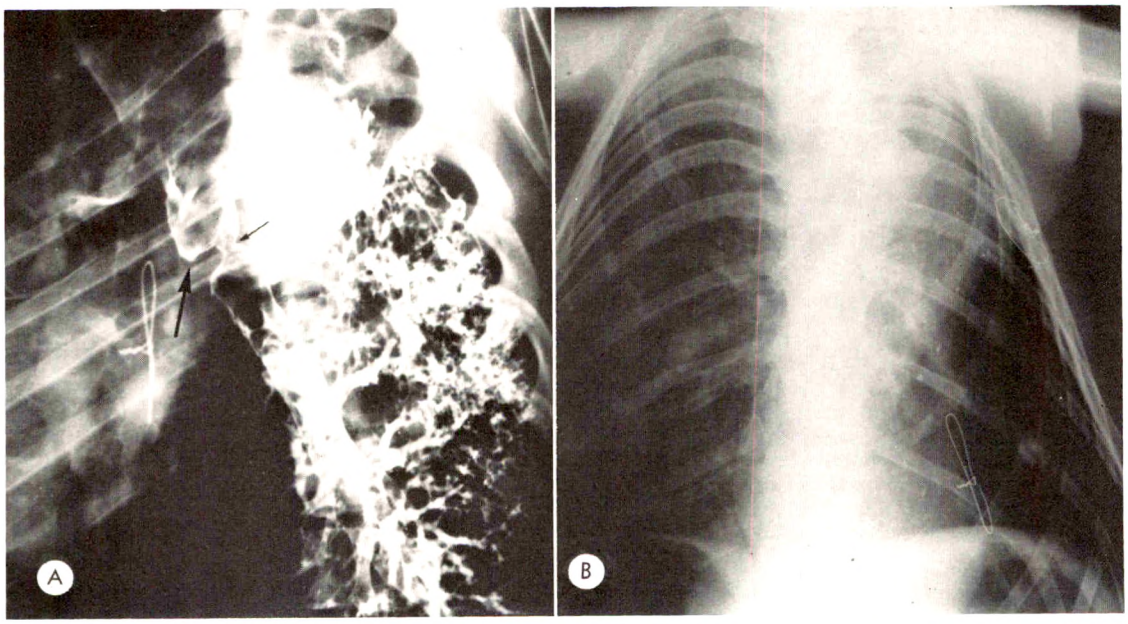


FIG. 2. Baboon No. 344. (*A*) Left bronchogram (right posterior oblique view) 10 weeks after reimplantation. There is a stenotic process distal to the bronchial anastomosis causing occlusion (large arrow) of the upper lobe bronchus, and marked narrowing (small arrow) of the lower lobe bronchus. (*B*) Roentgenogram showing left upper lobe atelectasis and residual contrast medium in the lung.

during the early postoperative period. One animal developed a localized empyema.

Stenosis distal to the bronchial anastomosis (Fig. 2*A*) was demonstrated in 3 animals that had bronchography. The bronchograms of the remaining animals were normal.

DISCUSSION

As an experimental animal in autotransplantation of the lung, the baboon is superior to the dog. Haglin[7] and his associates,[8] in a comparative study, reported that the mortality and morbidity rates, the function of the autograft, and the ability to survive contralateral pneumonectomy were uniformly better in the primate. Arnar and co-workers[1,2] noted that the baboon lung also tolerated well an extended ischemia time of up to 4 hours between harvesting and reimplantation.

The transient radiopacity of the reimplanted baboon lung is similar to that observed in the dog.[4,11] It is thought to represent edema, congestion and atelectasis. These were the changes found in the autografts of baboons that died postoperatively,[7] and, to a milder degree, in those of selectively sacrificed dogs that had uneventfully survived the reimplantation.[3] The edema or congestion appears to be related to interruption of the lymphatic drainage. In the dog, for example, roentgenographic evidence of resolution of the process is generally complete within a period of 2–3 weeks, coinciding with the time needed for regeneration of the lymphatic channels across the bronchial anastomosis.[6] The atelectatic component is presumably secondary to bronchial plugging by mucus or blood. The role of impaired surfactant activity should, however, also be considered. Such impairment has been demonstrated in the canine lung after unilateral ligation of the pulmonary artery or the bronchus.[10]

It should be emphasized that the roentgen picture described above is that of a primate lung reimplanted after an ischemia time of 1–3 hours, and most likely would not apply if the reimplantation were carried out immediately after extirpation. Extended ischemia is probably unavoidable in the harvesting of human cadaveric lung.

The incidence of pneumothorax was surprisingly high. The complication was attributed to leakage of air along the suture tracts of the bronchial anastomosis or through a pleural tear. The contralateral pneumothorax was thought to be the result of injury to the mediastinal pleura during dissection in the region of the left atrium.

Bronchostenosis has not been a common complication in the baboon. Its incidence in this series was 10 per cent, as compared to that of 18–61 per cent in the dog.[4,5,7] The stenosis may best be explained on the basis of local ischemia of the bronchus distal to the anastomosis.[4,7,11] It is believed that, after the lung is completely extirpated and then reimplanted, a collateral circulation develops between the pulmonary artery and the severed bronchial artery, bringing blood to the bronchus up to the line of anastomosis in a retrograde manner. Thus, an inadequate collateral circulation would lead to bronchial ischemia with subsequent stenosis. A further discussion on the bronchial complications following reimplantation of the lung will be published elsewhere.[12]

Autotransplantation of the lung is not without clinical applicability. It is the only sure method by which complete pulmonary denervation may be achieved, and may, therefore, be effective in the treatment of severe bronchial asthma, when all other measures have failed. Eight such operations have been performed by Meshalkin and associates[9] on 7 patients with intractable asthma. One had bilateral autografts in successive stages. Two patients died postoperatively, while all the others experienced marked symptomatic relief. Unfortunately the roentgenograms of these patients did not appear in the published report.

SUMMARY

In a group of 30 baboons the left lung was extirpated and, after a waiting period

of 1–3 hours, reimplanted. Postoperative roentgenograms at the end of 1 week showed a diffuse cloudiness throughout the lung, which resolved by the end of 4–6 weeks in the majority of cases.

Pneumothorax, either ipsilateral, contralateral, or bilateral, was noted in 14 animals. Stenosis of the anastomosed bronchus developed in 3 animals.

The incidence and cause of these findings are briefly discussed. The clinical applicability of pulmonary autotransplantation is described.

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REGIONAL PULMONARY BLOOD FLOW IN CYSTIC FIBROSIS*

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CYSTIC fibrosis is the most common chronic, nontuberculous lung disease in children. The degree of pulmonary involvement is of critical importance in determining the course, severity, and eventual outcome of the disease. Uncontrollable pulmonary infection and *cor pulmonale* are the most frequent causes of death.[7]

Pulmonary perfusion and ventilation scannings were performed in patients with cystic fibrosis. The purpose of this study was to improve our understanding of the pathophysiology of the disease and systematically test the potential usefulness of isotope scanning techniques in cystic fibrosis.

MATERIAL AND METHOD

Eighteen patients with proven cystic fibrosis were selected for this study. None of these patients had liver disease or chronic atelectasis. Their pulmonary status was stable, and none had any intercurrent acute disease at the time of lung scanning. Posteroanterior and lateral chest roentgenograms were obtained on the same day the scans were performed.

Xenon 133 lung scannings were performed on the older children and young adults. For the procedure the patient lay supine on a plastic-top table placed over an Anger camera; a mouth piece was connected through tubing and a three-way valve to a standard respirometer tank and an anesthesia bag. When the patient had adjusted to the respirometer system, 5 to 10 mc of xenon 133 was administered from the anesthesia bag with a single inspiration and rapidly washed in with 100 to 150 cc. of air. With the patient holding his breath for 10 to 20 seconds, a single-breath picture was made with the camera. Following this the patient exhaled and rebreathed the xenon 133 for 2 to 3 minutes into the respirometer system, after which an equilibrium picture was obtained. The valve was then changed to room air, and a series of wash-out pictures was obtained.

For the perfusion scans, 0.5 to 2 mc of technetium 99m labeled macroaggregates of albumin was administered with the patient still in the same position used for the xenon 133 studies. A scintillation picture of the posterior chest was then taken to compare with the xenon 133 scan. Following this, the scannings of the lungs were made using a standard rectilinear scanner. Anterior, posterior, and both lateral views were obtained.

Since considerable patient cooperation was required for the ventilation scannings, many of the younger children were unable to participate or complete the ventilation study. A total of 18 perfusion scannings and 10 complete ventilation scannings was performed.

RESULTS

Table 1 summarizes the clinical, roentgenographic and scanning data. The results of the pulmonary function studies are included in the table for reference.

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TABLE I

SUMMARY OF CASES

Patient	Age (yr.) and Sex	Clinical Status*	Chest Roentgenograms	Perfusion Scans	Ventilation Scans	Pulmonary Function Studies†
1 S.T.	1½ M	E	Within normal limits	Within normal limits		
2 D.B.	2¾ F	E	? Minimal RLL peribronchial thickening	Within normal limits		
3 J.B.	3½ M	E	Within normal limits	Multiple small perfusion defects		
4 C.M.	21 F	E	Within normal limits	Multiple perfusion defects primarily in upper lobes	Multiple ventilation defects, primarily in upper lobes	Mild airway obstruction. No restrictive disease
5 T.R.	4 F	E	Minimal diffuse peribronchial thickening	Perfusion defect RUL		
6 J.S.	3¾ M	E	Within normal limits	LUL perfusion defects		
7 R.C.	7¾ M	E	Slight RUL peribronchial thickening. Slight hilar lymphadenopathy	RUL slightly underperfused. Small LUL perfusion defect	RUL underventilated	Mild airway obstruction. No restrictive disease
8 T.C.	12¾ M	G	Moderate diffuse peribronchial thickening. Marked hilar lymphadenopathy	RUL under perfused. Small LUL perfusion defect	RUL underventilated. LUL slightly underventilated	Mild airway obstruction. No restrictive disease
9 D.G.	7¾ F	G	Slight diffuse peribronchial thickening. Moderate hilar lymphadenopathy. RUL bronchiectasis	RUL underperfused. Small LUL perfusion defect. Multiple small perfusion defects	RUL underventilated. RLL moderately underventilated	Moderate airway obstruction. Mild restrictive disease
10 R.G.	4¾ M	G	Diffuse peribronchial thickening. Slight hilar lymphadenopathy. RML bronchiectasis	Multiple large perfusion defects. Largest defect in the RML		
11 C.M.	17 F	E	RUL peribronchial thickening. Minimal hilar lymphadenopathy	RUL and LUL perfusion defects	RUL and LUL ventilation defects	Mild airway obstruction. No restrictive disease
12 S.F.	23 M	F	Marked diffuse peribronchial thickening. Multiple areas of bronchiectasis. Parenchymal nodules	Multiple large perfusion defects. Only the RLL remains well perfused	Marked underventilation of all lobes except the RLL	Moderate airway obstruction. Moderate restrictive disease
13 C.G.	8 F	F	Marked peribronchial thickening. ? Diffuse bronchiectasis	Large perfusion defect in RUL and LUL and ? LLL	Large ventilation defect in the upper lobes	Severe airway obstruction. Moderate restrictive disease
14 L.H.	21 M	P	Moderate hyperinflation. Marked peribronchial thickening. Slight hilar lymphadenopathy	Multiple large perfusion defects	Multiple large ventilation defects	Severe airway obstruction Severe restrictive disease

* In the assessment of clinical status the scoring system of Shwachman and Kulczucki[16] was slightly modified for the purposes of this study. E = Excellent. G = Good. F = Fair. P = Poor.

† In the assessment of pulmonary functions the following determinations were performed: FVC = forced vital capacity; FEV_1/FEV = forced expiratory volume; MVV = maximum volume ventilation; RV = residual volume; and RV/TLC = residual volume to total lung capacity ratio.

Abbreviations: RLL = right lower lobe; RUL = right upper lobe; RML = right middle lobe; LLL = left lower lobe; LUL = left upper lobe.

Table I—(*Continued*)

Patient	Age (yr.) and Sex	Clinical Status*	Chest Roentgenograms	Perfusion Scans	Ventilation Scans	Pulmonary Function Studies†
15 D.M.	13½ F	F	Slight hyperinflation. Moderate diffuse peribronchial thickening. Moderate hilar lymphadenopathy. Multiple areas of bronchiectasis	Marked underperfusion of RUL and perfusion defect in the LUL	Marked underventilation of both upper lobes	Moderate airway obstruction. Severe restrictive disease
16 R.R.	13¾ F	F	Moderate hyperinflation. Moderate diffuse peribronchial thickening. Hilar lymphadenopathy. RUL and LUL bronchiectasis	Extensive perfusion defects primarily in the upper lobes	Upper lobes underventilated	Severe airway obstruction. Moderate restrictive disease
17 M.S.	21 F	F–P	Marked hyperinflation. Marked peribronchial thickening. Multiple areas of bronchiectasis	Multiple large perfusion defects		Severe airway obstruction. Severe restrictive disease
18 E.T.	1 M	F–G	Within normal limits	? RUL perfusion defect		

For the purposes of analysis of the data, the 18 patients were grouped into 5 categories.

GROUP 1

Patients 1 (Fig. 1, *A–C*) and 2. Two small children, both under 3 years of age. Both in excellent health.* The chest roentgenograms were within the limits of normal, and the perfusion scans were negative. No ventilation scannings or pulmonary function studies† were performed on these children.

GROUP 2

Patients 3, 4, 5, and 6. Three small children, under 4 years of age and 1 young adult (Patient 4; Fig. 2, *A–C*). All 4 were in excellent health by clinical assessment. The chest roentgenograms in 2 (Patients 3 and 6) appeared to be within the limits of normal. In Patient 5 there was questionable involvement, and in Patient 4 there was definite but minimal involvement by roentgenography. The perfusion scans showed definite and localized perfusion defects in all these patients. In Patient 4 the perfusion defects correlated well with the ventilation defects, and the function studies showed very mild airway obstruction and no restrictive disease.

GROUP 3

Patients 7, 8 (Fig. 3, *A–D*), 9, 10, and 11. Four older children and 1 adolescent (Patient 11). Two of the 5 were in excellent health; 3 were in good health. All had positive chest roentgenograms, but the perfusion scans showed more extensive localized involvement in all than one would have suspected from the roentgenograms. The ventilation scans correlated well with the perfusion scans. The function studies showed marked to moderate airway obstruction, and only 1 (Patient 9) had any restrictive disease.

GROUP 4

Patients 12, 13, 14, 15, 16 (Fig. 4, *A–C*), and 17. One older child, 2 young teenagers, and 3 young adults. All were in only "fair" health, and at least 1 was in "poor" health (Patient 14).‡ All had extensive disease by chest roentgenograms, perfusion and ventilation scans alike. The perfusion and ven-

* Please see footnote under Table 1 for clinical classification and listing of pulmonary function tests.

† Pulmonary function studies were performed within 2 months of the date of the lung scannings.

‡ This is the only patient who has died since the completion of the study.

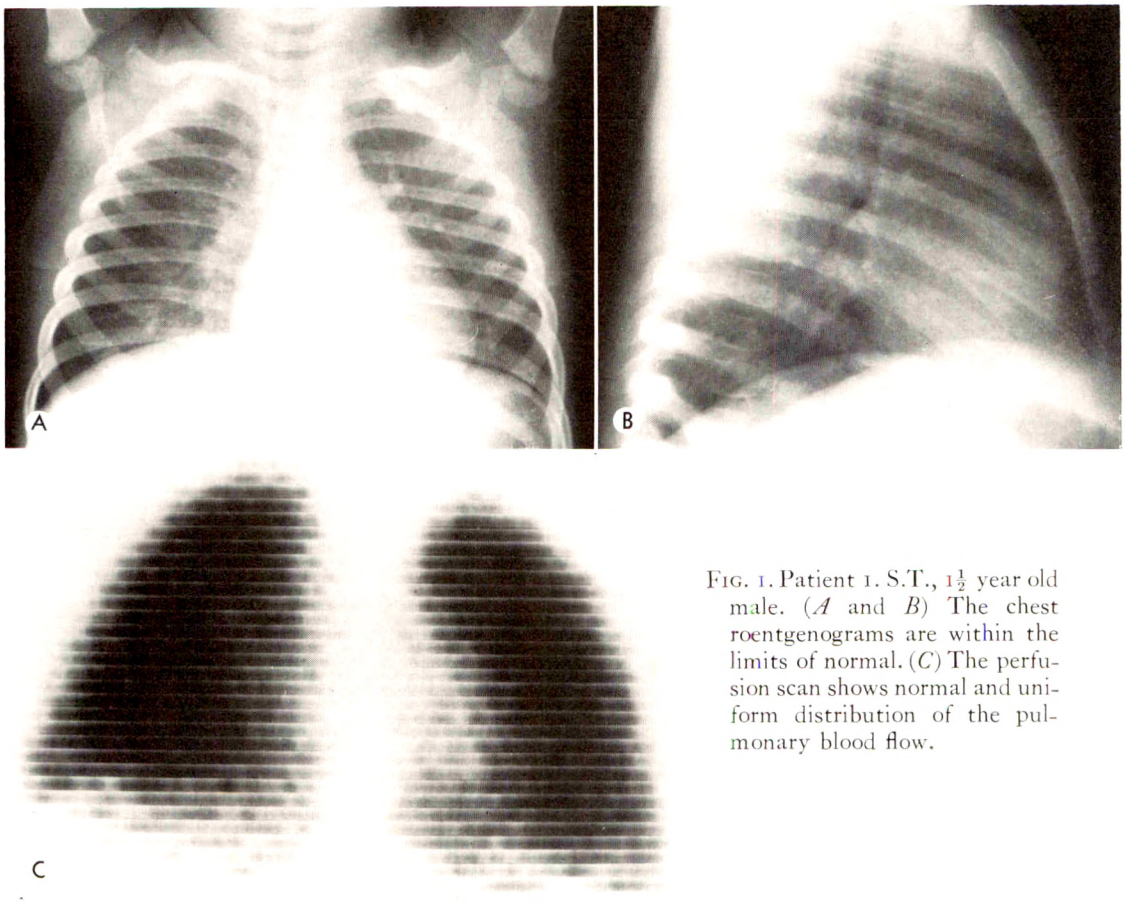


FIG. 1. Patient 1. S.T., 1½ year old male. (*A* and *B*) The chest roentgenograms are within the limits of normal. (*C*) The perfusion scan shows normal and uniform distribution of the pulmonary blood flow.

tilation scans correlated well: the underventilated areas were underperfused. All these patients had at least moderate airway obstruction and moderate to severe restrictive disease by function studies.

GROUP 5

A 1 year old infant. This patient did not fit into any of the groups. Clinically he was in only fair health. Although the chest roentgenogram appeared to be normal, there were several episodes of repeated respiratory infection, and at various times there was clear evidence of diffuse airway obstruction as demonstrated by air trapping and tracheal collapse on chest fluoroscopy. The perfusion scan showed a right upper lobe defect, when the child was free of acute disease.

DISCUSSION

A. THE PATHOPHYSIOLOGY OF THE LUNG INVOLVEMENT IN CYSTIC FIBROSIS

The basic abnormality appears to be the production of physically abnormal mucus.[1,7] The presence of this thick, tenacious material leads to obstruction and infection of the subsegmental bronchi. Repeated, acute obstructive-inflammatory episodes lead to chronic infection, peri- and intrabronchial fibrosis and bronchiectasis. Initially the process favors the upper lobes, but, as it progresses, its distribution becomes random. Gross destruction of the pulmonary parenchyma and capillary bed is not a feature of cystic fibrosis.[3] Apart from the small parenchymal abscesses the disease remains confined to the airways

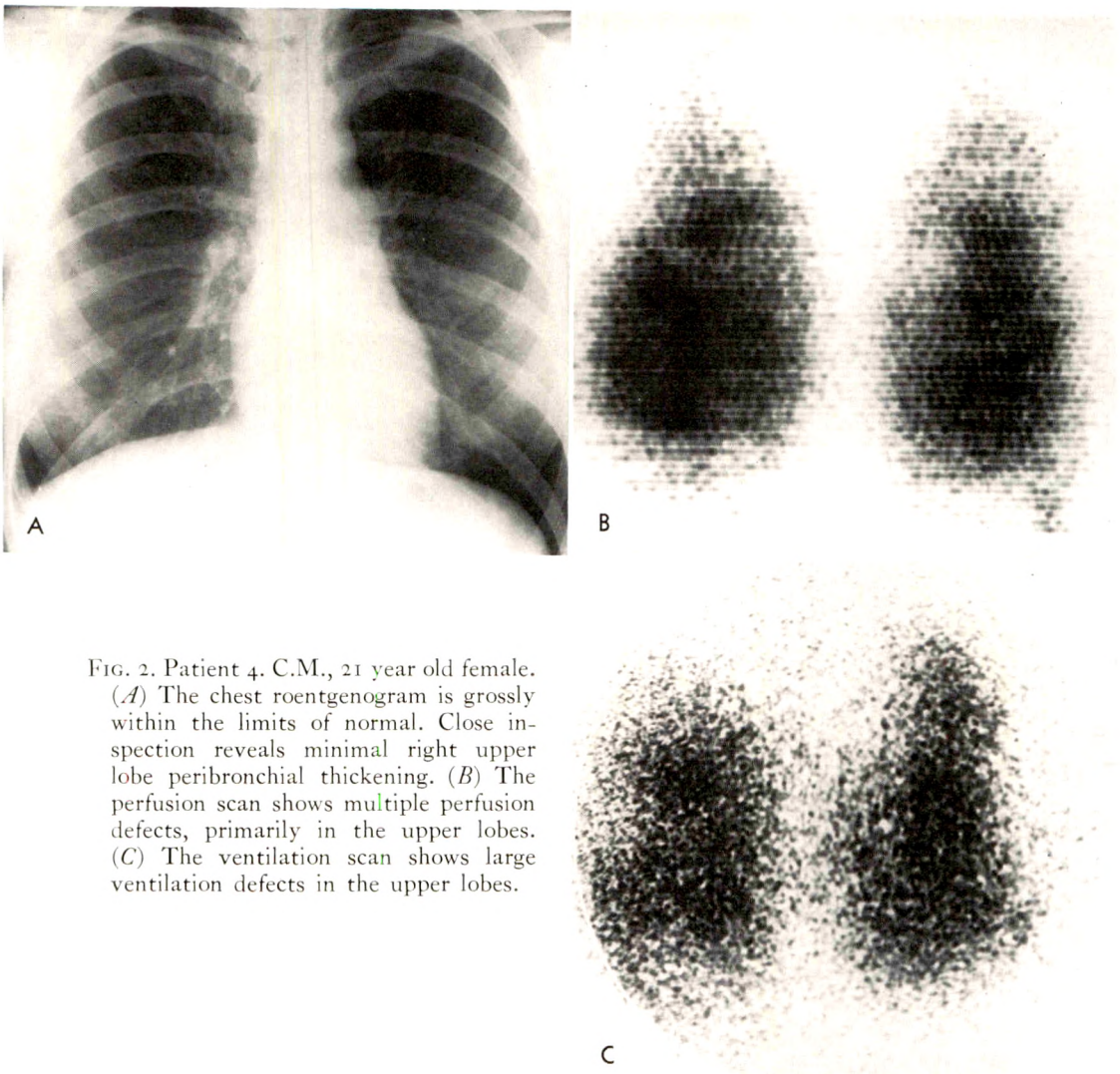


Fig. 2. Patient 4. C.M., 21 year old female. (*A*) The chest roentgenogram is grossly within the limits of normal. Close inspection reveals minimal right upper lobe peribronchial thickening. (*B*) The perfusion scan shows multiple perfusion defects, primarily in the upper lobes. (*C*) The ventilation scan shows large ventilation defects in the upper lobes.

even in its advanced form. As it becomes more extensive, the characteristic pattern of "obstructive pulmonary disease" emerges. The resulting ventilatory dysfunction is reflected by the abnormal pulmonary function studies: the vital capacity and ventilatory flow rates decrease, while the residual volume and airway resistance increase, as does the residual volume to total lung capacity ratio.[2,5,7,9,20] The intercurrent episodes of acute infections further worsen the ventilatory dysfunction.

A small number of patients with cystic fibrosis have undergone cardiac catheterization.[8,13,14] The available hemodynamic data suggest that in patients with advanced cystic fibrosis, pulmonary hypertension and varying degrees of hypoxemia accompany the abnormal airway dynamics.

B. The Meaning, Significance and Limitation of the Scans

The uneven distribution of intrapulmonary gas in cystic fibrosis has been repeatedly demonstrated by physiologic techniques.[6,9,12,19] The ventilation scan depicts and localizes the uneven distribution of the inhaled xenon 133, but it pro-

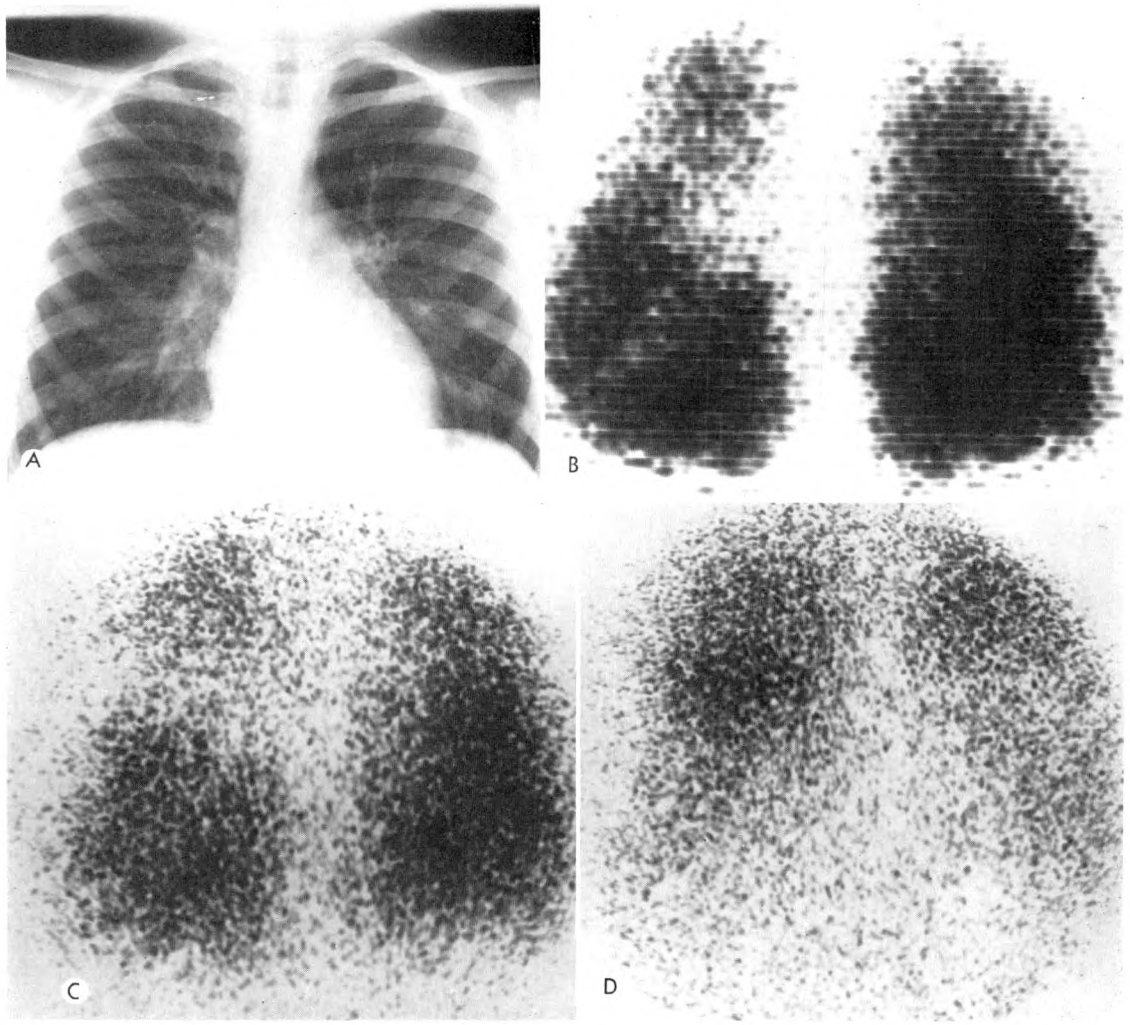


FIG. 3. Patient 8. T.C., $12\frac{3}{4}$ year old male. (*A*) The chest roentgenogram shows marked hilar lymphadenopathy and diffuse but mild peribronchial thickening. (*B*) The perfusion scan shows marked underperfusion of the right upper lobe and a small left upper lobe perfusion defect. (*C*) The ventilation scan shows marked underventilation of the right upper lobe and moderate underventilation of the left upper lobe. (*D*) The wash-out phase of the ventilation scan shows definite trapping of the tracer gas in the upper lobes, further indicating poor ventilation.

vides no explanation as to why various areas are *relatively* better ventilated than others; decreased ventilation, regardless of whether it is due to transient mucus plugs or extensive bronchial damage, appears as a ventilation defect on the scan. Similarly, the perfusion scan only shows that various areas are *relatively* better perfused than others.

The important finding in this series is the graphic demonstration that the underperfused areas are the *same* ones which are underventilated. This finding differs from previous concepts which suggested that the underventilated areas remain well or even overperfused.[3,8] Our findings are in accord with basic physiologic principles: as a region of the lung becomes underventilated, the resulting alveolar hypoxia causes arteriolar vasoconstriction, which diverts blood from the underventilated region.[4,11] Conversely, decreased blood flow in a given region of the lung results in localized bronchoconstriction and decreased ventila-

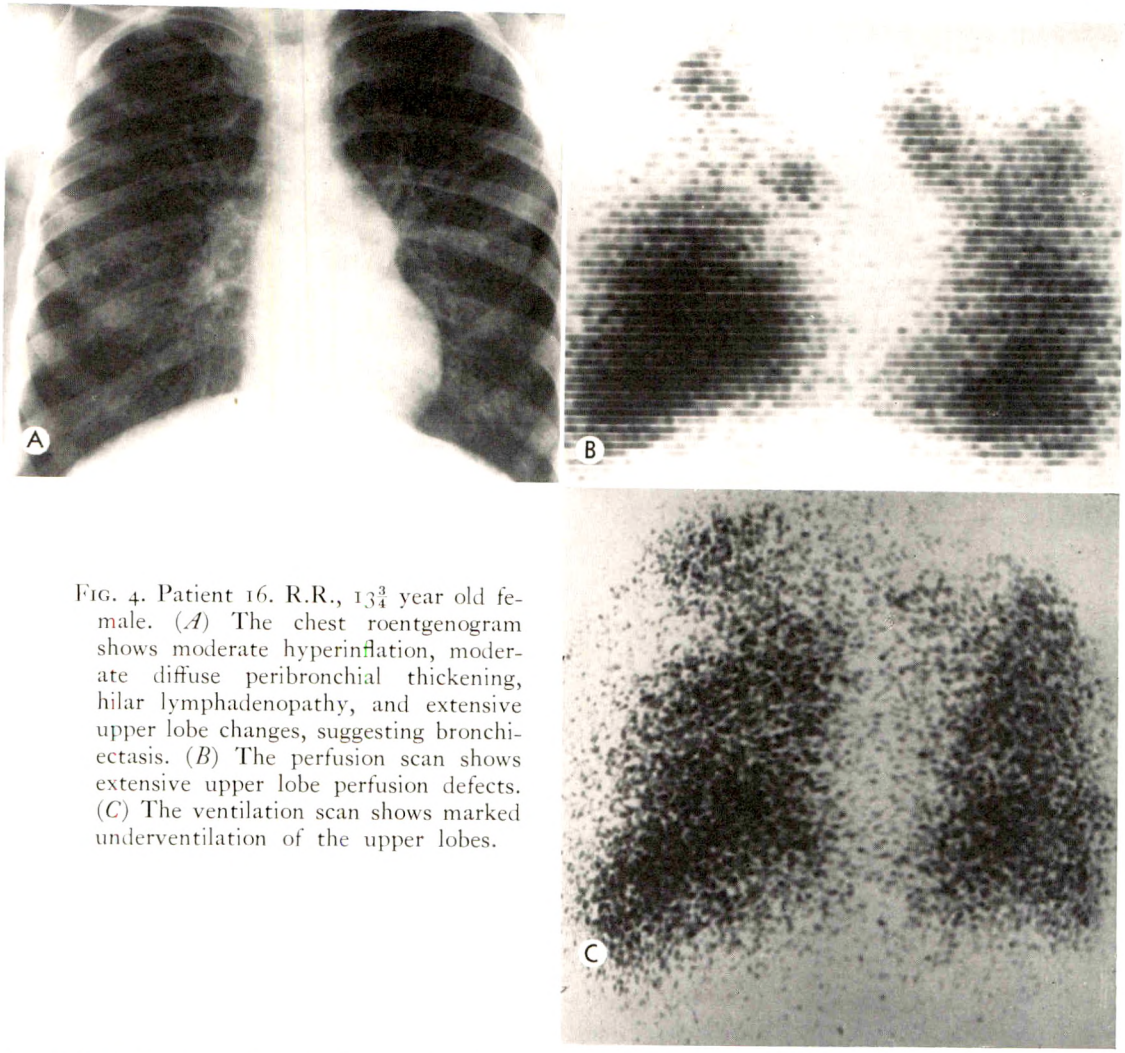


Fig. 4. Patient 16. R.R., $13\frac{3}{4}$ year old female. (*A*) The chest roentgenogram shows moderate hyperinflation, moderate diffuse peribronchial thickening, hilar lymphadenopathy, and extensive upper lobe changes, suggesting bronchiectasis. (*B*) The perfusion scan shows extensive upper lobe perfusion defects. (*C*) The ventilation scan shows marked underventilation of the upper lobes.

tion.[15,17] The matching perfusion and ventilation defects in our study reflect the presence and effectiveness of these regulatory mechanisms in cystic fibrosis.

The gas ventilation scans and the macroaggregate perfusion scans are not exactly comparable, quantitatively, and the resolving capabilities of scanning techniques are limited. While the scans demonstrate that underventilated areas are underperfused, this is qualitative information only. On the basis of the scans it is not possible to quantitate ventilation/perfusion ratios at the present time.

C. Roentgenologic Considerations

The chest roentgenogram plays a major part in the management of patients with cystic fibrosis. In the over-all clinical scoring of a patient with cystic fibrosis, the chest roentgenogram accounts for 25 per cent of the potential 100 points. The chest roentgenogram shows the progressive hilar lymphadenopathy, and detects bronchiectasis moderately well, even without bronchography. It shows the important small parenchymal abscesses excellently, and reveals acute superimposed infection far better than any other diagnostic method. In revealing hyperinflation in more advanced disease, it is a good indicator of increasing residual volume. Coupled with fluoroscopy, particularly in infants and small children, it reveals episodes of air trapping due to mucus plugs. In serial form and properly interpreted, the chest roentgenogram is an

invaluable asset. It shows primarily and best the *in vivo* anatomy of the disease.[10] It shows relatively little of the resulting functional abnormalities, which is one reason for the introduction of scanning techniques.

D. CLINICAL ASPECTS*

The clinician's efforts in managing cystic fibrosis are directed towards preventing, delaying, minimizing, and hopefully reversing the vicious cycle of the pulmonary involvement: obstruction—inflammation—bronchial damage—further obstruction, etc. The clinician must know which patient with cystic fibrosis has pulmonary involvement and how extensive it is. Early detection of pulmonary involvement is an obvious advantage.

If, as we assume, underperfusion reflects underventilation, then the perfusion scan might offer several advantages to the clinician: (1) It is easy to perform. With the use of an Anger camera it can be effectively and speedily performed even in non-cooperative infants. (2) It detects early involvement—often before it is clinically suspected or obvious on the chest roentgenogram. This is particularly true if scans are obtained in all 4 projections. Because it is such a sensitive method in detecting early involvement, it might become an excellent survey procedure to select patients for more extensive than routine preventive therapy. (3) It provides graphic delineation of the involved areas, and thus it localizes the disease for physical therapy and postural drainage. (4) It provides some information in regard to functional derangement caused by the pulmonary involvement. For this reason it might become a good method to evaluate the effectiveness of the therapy and to gauge the severity of the disease in advanced cases. (5) It does not appear to be detrimental to the patient. Apart from one pyrogenic reaction, we had no ill effects from technetium 99m macroaggregate scanning, even in advanced cases. As gas isotopes for perfusion scanning become more available and more widely used, even the theoretical danger of macroaggregate embolization will be eliminated.

Our initial experiences with lung scanning in cystic fibrosis are promising. Further studies are now required in this field; perfusion and ventilation scannings need to be performed in more patients. Also, perfusion and ventilation scans will have to be correlated with pulmonary function studies and chest roentgenograms more extensively before definite conclusions can be formulated. Nonetheless, these initial results appear to fully justify further studies.

* Detailed analysis of the clinical data and their relationship to pulmonary function studies and lung scans will be discussed in a forthcoming paper.

SUMMARY

The distribution of pulmonary blood flow was studied in 18 children and young adults with cystic fibrosis by pulmonary perfusion scanning. In addition, 10 of these patients also had ventilation scannings.

The perfusion and ventilation scans showed good correlation; underventilated areas were uniformly and persistently underperfused and *vice versa*. The physiologic significance of these results is discussed.

Perfusion scannings are easy to perform, even in small children. In this series the perfusion scan appeared to be more sensitive than the chest roentgenogram in detecting the presence and extent of early pulmonary involvement. The potential applications of scanning techniques in cystic fibrosis are discussed.

Pulmonary perfusion scanning promises to be a useful technique in the diagnosis and management of cystic fibrosis, provided that these initial results will be confirmed by further and more extensive studies.

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ANGIOGRAPHIC OBSERVATIONS ON THE TREATMENT OF PULMONARY THROMBOEMBOLISM WITH UROKINASE*

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IN RECENT years, 2 fibrinolytic activators, namely streptokinase and urokinase, have been investigated as to their value in the treatment of pulmonary embolic disease. Laboratory and animal investigations have been carried out by Browse and James,[1] Tow *et al.*,[14] Sherry,[11] and Hume.[7] In man, urokinase appears to be the superior of the 2 agents because of lack of pyrogenic activity and greater predictability of dosage response.[5] Both agents activate profibrinolysin (plasminogen) leading to the appearance of fibrinolysin (plasmin) in the blood. Fibrinolysin adheres to fresh thrombus material and reduces the fibrin to soluble fragments leading to resolution. The complete process is a complicated one in that the breakdown products may act to inhibit further activation of profibrinolysin. There are other aspects of this interaction which will be mentioned later. Urokinase became available for use in patients in 1966.* Sautter *et al.*[9] reported on its use in 10 patients in whom the diagnosis was strongly suspected from the history and clinical findings and was confirmed by pulmonary angiography. The progress of the patients was documented by clinical observation, pulmonary arterial pressures and follow-up pulmonary angiography carried out as early as 14 to 24 hours following urokinase treatment. The results of treatment based on angiographic observations were reported as excellent in 3, good in 3, fair in 2, and poor in 2 cases. In contrast, clinical improvement was reported as excellent in 8 and good in 2 cases. The urokinase was administered as a loading dose of 1,650 CTA units per pound of body weight delivered in a 10 minute period, and an equal amount was given each hour for 8 hours. In most instances, a peripheral vein was used for the infusion; however, in a few, but unspecified number, the drug was administered through the catheter in the pulmonary artery.

Sasahara *et al.*[8] reported on 8 patients treated in much the same manner. Documentation of progress was obtained by multiple scans in 4 projections, angiography, pulmonary function studies and clinical observations. Follow-up angiography was performed in some cases as early as 10 to 16 hours after the administration of urokinase. The results were judged as excellent in 1 case, good in 1, fair in 3, minimal in 2, and none in 1. All of the patients appeared to respond clinically, and in most instances there was an immediate improvement (1 to 3 days) on the lung scan, but the angiographic studies did not parallel these observations.

Tow *et al.*[13] reported on the treatment of 13 patients given urokinase in whom the progress was assessed by repeated lung scans, the first of which was made at 24 hours following the beginning of treatment. The results were judged as excellent in 5 cases, good in 2 and no response in 6. In those with an excellent response, the scan changed significantly in 24 hours, and this was compared with previous observations on 69 patients not treated with urokinase (all patients received heparin) in whom changes required at least 4 days to appear.

In all of the above reports, the patients

* Manufactured by Sterling, Winthrop and by Abbott Laboratories.

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appeared to be suffering from relatively acute pulmonary thromboembolism. Duration of symptoms varied from a few hours to 2 weeks, although some of the patients had had previous evidence of embolization. The response to treatment appeared to correlate to some degree with the duration of the symptoms. Urokinase was administered in much the same manner in all of the cases, except a few of those treated by Sautter *et al.*[9] in which the drug was administered by intrapulmonary catheter. This consisted of a preliminary loading dose of approximately 1/4 million units followed by an infusion of urokinase lasting up to 8 to 9 hours. Complications attributed to the drug were hematoma formation at the puncture site, oozing from the gums, and slight vaginal bleeding, all of which were inconsequential. In the series of Tow *et al.*,[13] 6 patients were allowed to pass through a control period of 8 to 12 hours, during which the only specific treatment was heparin. During this time, no favorable change was noted in the patients' condition. However, within 24 hours of the beginning of urokinase therapy, significant changes on the lung scans appeared. In most of the patients mentioned in all 3 series, heparin was given during the course of the treatment.

Dickie *et al.*[2] explored a different regimen for the administration of urokinase in 2 patients. Both of these patients suffered from massive embolization, and the diagnosis was established by pulmonary angiography. Urokinase was administered through the same catheter used for pulmonary angiography. The urokinase was administered over a 6 to 10 minute period A second or third dose of approximately the same size was given at 24 and/or 48 hours, depending on the progress of the condition. There was an immediate and striking resolution of the thromboemboli in both cases. It was suggested that the relatively rapid administration of the urokinase in a single dose offered a better activation of the proenzyme absorbed on the fibrin in the thromboembolus.

MATERIAL AND METHOD

Eleven patients with pulmonary thromboembolism have been treated with urokinase. All patients had signs or symptoms within 14 days of the beginning of the treatment, although 5 patients had a history compatible with the disease extending back months or years. One patient was eliminated from the study because he was not treated according to our protocol. This patient recovered.

Our protocol consisted of the establishment of a diagnosis by means of selective pulmonary angiography performed as soon as possible after the onset of signs and symptoms. Pulmonary pressures and cardiac outputs using dye dilution techniques were determined at intervals during the first 72 to 96 hours. Urokinase in a single dose of 15,000 units per kg. of body weight was instilled in a period of 6 to 10 minutes through the catheter that had been inserted into the main pulmonary artery. Repeat pulmonary angiography was performed at approximately 24 and 48 hours after treatment and again in 5 to 7 days. In 7 cases, additional angiography was performed at approximately 72 hours. A number of lung scans were carried out, but these were not a part of the protocol. Assays for coagulation and fibrinolytic elements of the blood were performed on all patients. These included determinations of fibrinogen, prothrombin, Stypven time, partial thromboplastin time, prothrombin consumption, euglobulin lysis time, and cold fibrinolytic potential. The pulmonary artery pressures and electrocardiograms were monitored continuously for periods of up to 72 hours. Our method of administration of the urokinase differs in most instances from that of the other workers mentioned above in that we administered it in a single dose over a period of 6 to 10 minutes through the catheter placed in the main pulmonary artery. Sautter *et al.*[9] mention the use of this route but do not give the number of patients so treated. The intent was to produce a high concentration of the agent in the region of the clot with consequent

better adherence of the active element to the clot. Another difference was in the regular use at daily intervals of selective pulmonary angiography to evaluate the progress of the case. A total of 44 angiographies was done in the 10 patients, and in only 1 was there any significant reaction to the procedure. This is mentioned in the report of Case 1. The age of the patients varied from 38 to 81 years.

TECHNIQUE

Selective pulmonary angiography was carried out by the injection of 40 cc. of renovist* injected through a NIH catheter placed in the main pulmonary artery at a pressure of 400 pounds per square inch. Injection times varied from 1 1/2 to 2 1/4 seconds. Films were exposed in a single plane on a Schönander film changer at the rate of 3 per second for 4 seconds and then 1 per second for 7 seconds. The initial series was usually exposed to best show detail in the large hilar arteries and the pulmonary trunk. The subsequent angiograms were exposed with slightly less radiation in order to better examine the peripheral lung vessels. In assessing changes, an attempt was made to standardize the angiographic procedure in order to provide comparable studies. Comparisons were carried out with angiograms made in the same phase or at comparable times during the filming process. Comparison of degrees of filling of large and medium-sized pulmonary arteries requires that the angiograms represent the same stage of filling, and it is essential to review an entire series of angiograms before selecting those for comparison.

The results of the laboratory studies and the hemodynamic findings will be the subject of separate reports.

RESULTS

The results are summarized in Table 1. The cases may be divided into 3 groups, those with good to excellent, those with partial or incomplete, and those with no significant detectable response. These represent Cases 1 to IV, V, VII and IX and Cases VI and X, respectively (Table 1). In 1 case (Case VIII), the observations were incomplete because the patient, although improving, was withdrawn from the study.

A good to excellent response consisted of a rapid decrease in dyspnea, return of peripheral blood pressure and pulse to the preembolic levels accompanied by a decrease in pulmonary artery pressure and resistance, and angiographic evidence of diminished size or disappearance of large proximal thromboemboli. These changes began within a few hours of the administration of the urokinase and usually progressed so that at the end of 7 to 9 days there was little if any evidence of the previous gross emboli.

A partial or incomplete response was indicated by a recognizable decrease in the size of the thromboemboli angiographically, which occurred within 24 to 48 hours. However, the emboli persisted and were visible at the end of 7 to 9 days of observation. Some degree of dyspnea and other signs of impaired pulmonary circulation usually persisted, even though the pulmonary artery pressure became or approached the normal. We do not have angiographic studies beyond 9 days in these patients, although subsequent lung scans show that underperfusion persisted in those segments where the emboli were known to have been present.

Minimal response was indicated by persistence, for a period of 7 to 9 days, of gross thromboemboli in the larger pulmonary arteries. The contour of these thromboemboli might have changed slightly during the period of observation, but the change was insignificant. Likewise, the patient's clinical condition did not show any dramatic change, and the pulmonary artery pressure and pulmonary resistance remained slightly elevated and in the range observed prior to treatment.

In none of the patients did we have previous angiograms or lung scans prior to the immediate period of observation. In those

*E. R. Squibb & Sons, Inc.

TABLE I

SUMMARY OF CASES

	Patient Age Race Sex	Primary Diagnosis	Duration of Signs and Symptoms of Pulmonary Thromoembolism	Duration of Most Recent Symptoms	Pulmonary Angiogram	Pulmonary Artery Pressure (mm. Hg)	Urokinase Administered (units $\times 10^3$)	Follow-Up
I*	V.McL. 47 W.F.	Postoperative hysterectomy	8 hr.	8 hr.	80 per cent obstruction of all lobar arteries of right lung; 30 per cent peripheral perfusion; massive obstruction of left pulmonary artery with 10 per cent peripheral perfusion	38→20 2 hr.	990 initial, 630 17 hr.	Marked clearing of lobar arteries, 48 hours; complete clearing, 9 days; some peripheral underperfusion of left base
II*	W.T. 59 W.M.	Postoperative iliac vein graft	6 hr.	6 hr.	Partial obstruction of upper lobe artery on right; 70 per cent peripheral perfusion; obstruction of all lobar arteries on left; 10 per cent peripheral perfusion		1,250 initial, 940 19 hr., 1,050 5 da.	Marked clearing of right upper lobar artery, 48 hours; subsequent embolus to left main artery, 49 hours; complete clearing, 6 days
III*	A.L. 52 N.M.	Postoperative iridectomy, 7 days	4 hr.	8 hr.	Minor obstruction of right upper lobe artery; 90 per cent obstruction of middle and lower lobe arteries; minor obstruction of left upper lobar artery; 60 per cent obstruction of lower lobar artery		1,000 initial, 500 24 hr.	Definite clearing, 24 hours; complete clearing in lobar arteries, 72 hours; some peripheral underperfusion on left at 8 days
IV*	R.P. 54 N.M.	Postoperative cystostomy	36 hr.	36 hr.	50 per cent obstruction of right upper lobar artery; occlusion of middle lobe artery; diminished perfusion of right base artery; 70 per cent obstruction of left lower lobar artery		710 initial, 750 20 hr.	Clearing of lobar arteries, 48 hours; segmental arteries of left base contained visible emboli; cleared, 7 days
V*	E.P. 55 N.M.	Fracture of ankle	12 da.	1–2 da.	Right upper lobar artery 80 per cent obstructed; peripheral perfusion 20 per cent; left upper lobar artery 90 per cent obstructed; left lower lobe artery 40 per cent obstructed; peripheral perfusion 30 per cent	31→18	1,500 initial, 840 21 hr.	Right upper lobar artery improved, 24 hours; 10 per cent obstruction, 5 days; peripheral perfusion 50 per cent; left upper lobe improved, 24 hours, cleared in 5 days; left lower lobe gross emboli resolved; still attenuated; peripheral perfusion 80 per cent
VI*	F. B. 38 N.M.	Myocardial infarction, heart failure	months?	3 da.	Segmental obstruction of right lower lobe artery; massive obstruction of left pulmonary artery	50→43	1,260 initial, 1,260 19 hr.	No significant change, 7 days
VII	L.H. 32 N.M.	Gunshot wound of thigh	5 wk.	1 da.	50 per cent narrowing of right upper and right lower lobar arteries—saddle embolus; peripheral perfusion 50 per cent; 20 per cent obstruction of left upper lobar artery; 50 per cent obstruction of segmental arteries of left lower lobe; peripheral perfusion 50 per cent	25→12	1,500 initial, 715 46 hr.	Right upper and right lower lobar arteries improved, 24 hours; normal, 6 days; peripheral perfusion 90 per cent; left upper lobar arteries improved, 6 days; left lower lobe segmental arteries improved, 48 hours; peripheral perfusion 60 per cent
VIII	T.L. 48 W.M.	Arteriosclerotic heart disease, pulmonary fibrosis, diabetes	12 da.	12 da.	Right intralobar arteries narrowed; peripheral perfusion 30 per cent; embolus of left pulmonary artery; peripheral perfusion 40 per cent; extensive fibrosis of both lungs		1,170 initial, 1,170 24 hr.	Study discontinued by private physician; patient improved symptomatically
IX	W.U. 67 N.M.	Hypertension, heart failure, obesity	1 mo.	1 da.	Attenuation of right lower lobar segmental arteries; peripheral perfusion 70 per cent of normal; embolus; left upper lobar artery 80 per cent obstructed; left lower lobar artery 50 per cent obstructed; peripheral perfusion 50 per cent	23→10	1,835 initial	Minimal change in right lung, 7 days; peripheral perfusion unchanged; left upper lobar embolus largely disappeared, 24 hours; left lower lobar embolus disappeared, 48 hours; peripheral perfusion diminished, particularly at left base, 7 days
X	I.F. 81 N.M.	Hypertension, congestive heart failure	1–4 da.	1–4 da.	Peripheral perfusion diminished to right lower lobe; amputation of left lower segmental artery, probably embolus; lower lobe perfusion markedly diminished		1,260 initial	No significant change, 24 hours

* Case reports presented in the text.

in which no detectable change occurred, some question exists as to the duration of the thromboemboli. It can be seen in Table 1 that in the patients in these groups the symptoms were intermittent and of longer duration, and it seems likely that we were dealing with one of the episodes of a chronic recurring embolization. In 2 in-

stances, there was angiographic evidence of fresh or new embolization during the course of treatment (Cases I and II).

Cases I and II have been the subject of a previous report.[2]

REPORT OF CASES

EXAMPLES OF GOOD TO EXCELLENT RESPONSE

CASE I. A 47 year old white female underwent abdominal hysterectomy on February 13, 1967 because of uterine fibroids. Her postoperative course was uneventful until the 6th day when she developed signs and symptoms of thrombophlebitis in both calves and complained of aching in the costovertebral angles. Early in the morning of the 9th postoperative day, she suddenly became dizzy, and this was followed by a substernal choking sensation and a feeling of pressure over the anterior chest. The pulse was 90 per minute and blood pressure 110/70. Within 4 hours, the pulse was 120 per minute, and the blood pressure was 90 systolic during the administration of intravenous angiotensin. Electrocardiogram showed right heart strain.

Nine hours after the sudden onset of symptoms, a catheter was placed in the pulmonary artery, pressures were recorded, and pulmonary angiography was carried out (Fig. 1*A*). Large thromboemboli were seen in the main pulmonary artery and in both the right and left branches. These were estimated to obstruct more than 50 per cent of the cross-sectional area of the pulmonary arterial system, and this was supported by the large area of lung parenchyma that was underperfused. Immediately following pulmonary angiography, the heart stopped beating for about 1 minute, and this was ac-

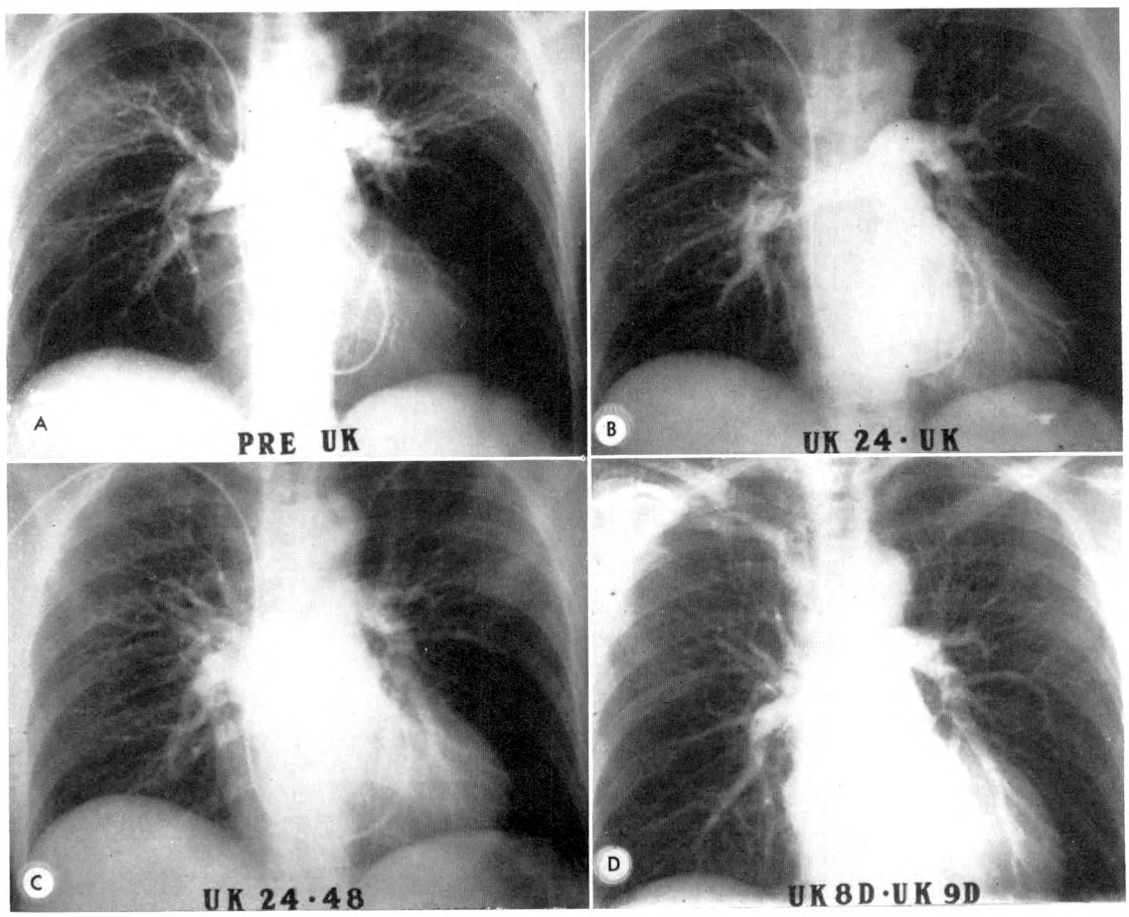


FIG. 1. Case I. Example of excellent response. (*A*) Angiogram 9 hours after onset of symptoms. Mean pulmonary artery pressure was 38 mm. Hg, and patient was in mild shock. (*B*, *C* and *D*) Selected angiograms performed at 24 and 48 hours and 8 days following first dose of urokinase. The gross emboli had disappeared in 48 hours.

companied by a mild seizure. Following closed chest massage, the heart resumed a regular rhythm, and the patient quickly returned to her previous state.

Eleven hours after the onset of symptoms, 990,000 units of urokinase were instilled through the catheter in the pulmonary artery. Within 1 hour, the blood pressure stabilized at 100/80 without angiotensin, and the pulmonary artery pressure had fallen from a pretreatment level of 51/21, mean 33, to 35/12, mean 23 mm. Hg. Within another 30 minutes, the peripheral blood pressure stabilized at the previous average levels for the patient. Four hours after the initial treatment, the patient again noted chest pain, dyspnea, nausea and vomiting. The blood pressure and pulmonary artery pressure remained unchanged. Within 24 hours (Fig. 1*B*), the large thromboembolus in the right pulmonary artery had decreased in size, and at 48 hours (Fig. 1*C*) it was no longer recognizable. The peripheral arteries were still more sparse than normal, but this was difficult to evaluate. On the left side, the lower lobe arteries had become patent. Several of the smaller arteries were truncated, and the number of peripheral arteries was definitely decreased. The patient had an uneventful convalescence and left the hospital on the 18th day and 12 days after the onset of her acute attack of thromboembolism. On the last pulmonary angiogram (Fig. 1*D*), the pulmonary vascular system was judged to have returned to approximately normal appearance. Lung scans on the second and fifth days showed marked improvement.

Comment. This patient appears to have been an example of an acute onset of massive pulmonary thromboembolism, for which treatment was carried out within 11 hours of onset. There was an immediate and dramatic decrease in the size of the proximal pulmonary emboli and a decided improvement in the peripheral perfusion of the lung. The peripheral lung may have still been underperfused, as evaluation of peripheral circulation is quite difficult without comparative studies representing the normal state.

Case II. W. T., a 59 year old white male, underwent a right iliofemoral dacron bypass graft on February 14, 1967. On the 11th postoperative day, the patient had a sudden onset of dyspnea followed in a short time by hemoptysis and a friction rub in the right lower chest. Pulse was 84 and blood pressure 100/70. Approximately 10 hours after the onset of symptoms, selective pulmonary angiography was done (Fig. 2*A*), and following this 1,250,000 units of urokinase were injected into the pulmonary artery over a period of about 10 minutes. The initial pre-urokinase angiogram showed some obstruction to the upper lobe branch of the right pulmonary artery and slight obstruction in the artery to the middle lobe, with only a minimal degree of underperfusion of the peripheral arteries. On the left side, there were numerous small radiolucencies in the descending branch of the pulmonary artery, and there was poor peripheral perfusion of both the anterior branch of the upper lobe and all of the lower lobe. At 24 hours (Fig. 2*B*), following the first dose of the urokinase, there was a striking change in the size of the embolus in the upper lobe of the right lung, and the peripheral perfusion was improved. On the other hand, on the left side the peripheral perfusion was much reduced, and the upper lobe artery was scarcely filled. A second dose of 940,000 units of urokinase was given. An angiogram done the following day showed that the obstruction to the left artery had increased further, and the peripheral perfusion was greatly diminished. There was a second negative shadow in the main pulmonary artery suggestive of a second embolus. In fact, the evidence would suggest that there had been continued further embolization to the left pulmonary artery (Fig. 2*C*). On the 5th day following the first treatment, a selective angiogram (Fig. 2*D*) showed a very considerable improvement in the peripheral perfusion, but several obstructed areas were noted in the branches to the lower lobe. Consequently, at 5 days another dose of 1,050,000 units of urokinase was given. On the following day another selective angiography was carried out, and this showed what was thought to be a completely normal pulmonary arterial system (Fig. 2*E*). There was now no evidence of any emboli. The mean pulmonary artery pressure was 9 mm. Hg, and the patient was symptomatically much improved.

Comment. There is good evidence that further embolization occurred after the first dose of the urokinase. This resulted in almost complete occlusion of the left pul-

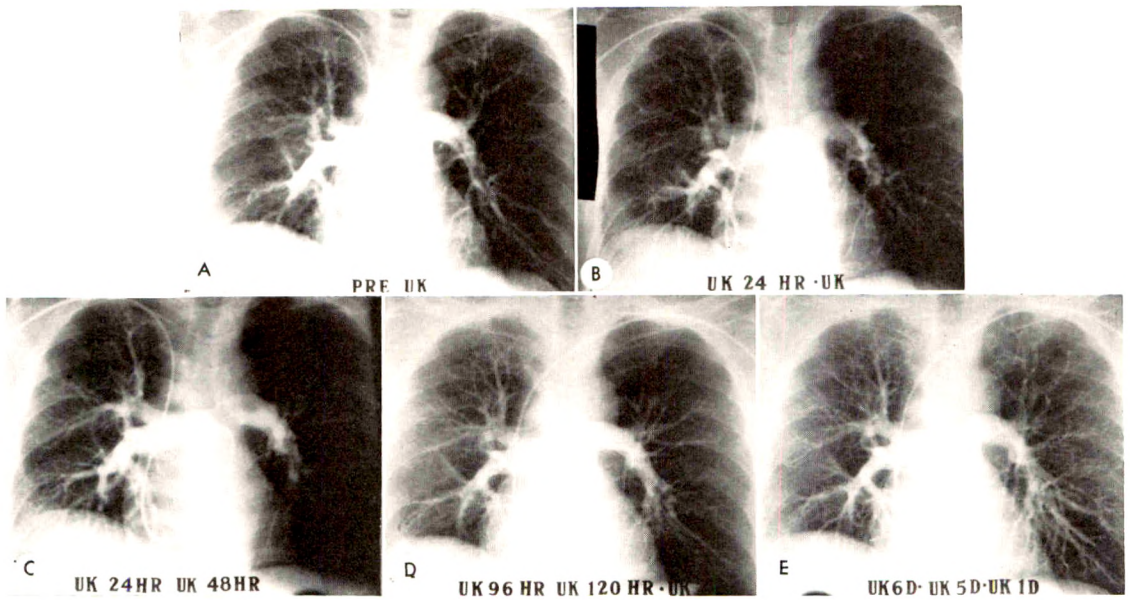


FIG. 2. Case II. Example of excellent response. (*A*) Angiogram 10 hours after sudden onset of symptoms. (*B*) Angiogram at 24 hours after single dose of urokinase. The embolus in the right upper lobe artery is smaller, but the massive embolus in the left pulmonary artery is larger. A second dose of urokinase was given. (*C*) Angiogram at 48 hours after beginning of treatment. The embolus in the left pulmonary artery is larger resulting in almost complete occlusion. There was evidence of an additional embolus in the left pulmonary artery. The pulmonary artery pressure remained mildly elevated (17 mm. Hg), and the patient had clinical evidence of further embolization. Urokinase was not administered because of the possibility that it might have something to do with the dislodgement of other thrombi. (*D*) Angiogram at 5 days showing marked improvement. Another dose of urokinase was given. (*E*) Angiogram at 6 days showing complete clearing of all of the gross emboli with return to normal appearance of the pulmonary arterial system.

monary artery. However, there was a rapid resolution of these thrombi, and at the end of 4 days following the second dose of urokinase, the pulmonary vascular system on the left side had returned entirely to normal.

CASE III. A. L., a 52 year old Negro male, had a peripheral iridectomy of the left eye on March 26, 1968 because of granulomatous uveitis, and the operation was repeated on the following day. The patient was confined to bed for 4 days. On April 3, 1968 he went to the toilet and collapsed. Immediately thereafter, the blood pressure was barely obtainable at 40/0, and the pulse was 120 and irregular. The patient was given O_2, aramine and heparin. He responded to a degree and showed marked dyspnea and anterior chest pain. A selective angiogram (Fig. 3*A*) showed extensive embolization of the greater part of the right pulmonary artery except for a few small branches to the anterior and apical segments of the lower lobe. There was almost no perfusion of the lower and middle parts of the right lung. On the left side, a large thromboembolus lay near the origin of the descending branch, and it was faintly outlined with a ghost-like shadow. The lingular branches were truncated, and the upper lobe branches were poorly perfused. Immediately following the pulmonary angiography, 1 million units of urokinase were instilled into the pulmonary artery over a period of about 10 minutes. A pulmonary scan on the same day showed marked underperfusion of the left lower lung but little change in the right lung.

Twenty-one hours later, a second angiogram showed increased perfusion of the upper and lower lobes of the right lung (Fig. 3*B*). The large embolus in the descending branch of the left pulmonary artery had decreased markedly in size leaving only a spherical shadow in the anterior arterial branch to the lower lobe. The pulmonary artery mean pressure had dropped from 15 to 8 mm. Hg, and the cardiac output had increased. The patient was given an additional 500,000 units of urokinase, and angiography performed on the following day (approxi-

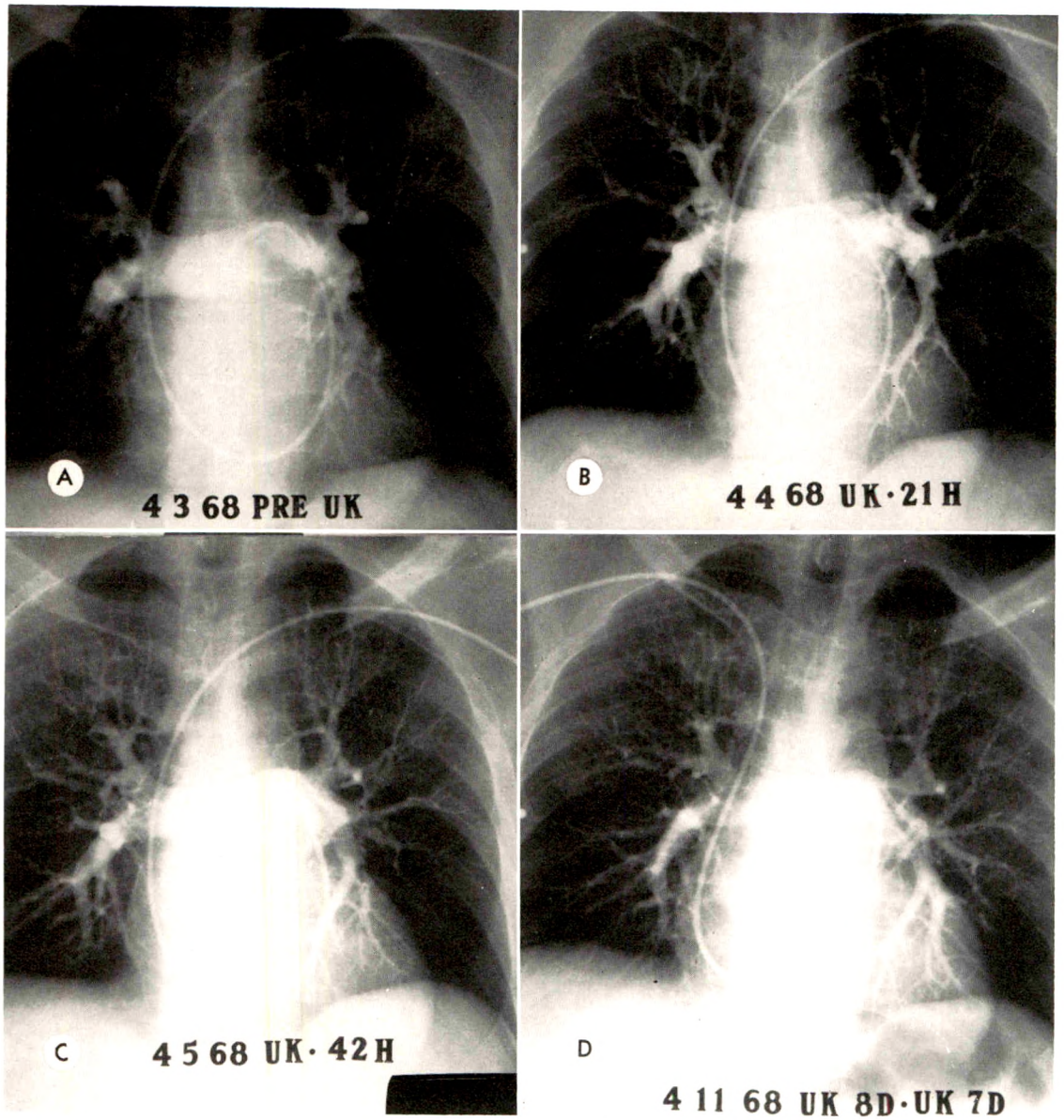


Fig. 3. Case III. Example of good response. (*A*) Angiogram 4 hours after sudden onset of symptoms. Mean pulmonary artery pressure was 15 mm. Hg. Peripheral blood pressure was 40/0. (*B*) Angiogram 21 hours after first dose of urokinase. There had been a striking reduction in size of the thromboemboli in both the right and left pulmonary arteries, and the pulmonary artery pressure was 9 mm. Hg. A second dose of urokinase was given. (*C*) Angiogram 42 hours after beginning of treatment. A small oval-shaped shadow in the lateral portion of the lower lobe pulmonary artery is the residual of the much larger embolus seen 42 hours before. (*D*) Angiogram at 8 days shows clearing of all gross emboli. There is still underperfusion at left base.

mately 42 hours following the first treatment) showed a further increase in perfusion of the right upper lobe (Fig. 3*C*). The spherical shadow in the descending branch of the left lower lobe persisted but was smaller. A posterior lung scan on the following day (approximately 70 hours after the onset of treatment) showed marked improvement over that of 2 days before, and only the left base remained underperfused. Another angiogram on the 8th day following treatment showed no gross emboli and the spherical embolus had resolved,

but the left base was underperfused (Fig. 3*D*). This was confirmed by the scan of the previous day. The pulmonary artery pressure and peripheral resistance had dropped, and the cardiac output was normal. The patient made an uneventful convalescence and has remained well for 4 months.

Some bleeding occurred around the site of the catheter insertion, but this was easily controlled.

Comment. The first attack of massive pulmonary thromboembolism produced quite definite symptoms. The diagnosis was made within a few hours, and treatment with urokinase was instituted. There was a prompt and striking decrease in the size of the pulmonary emboli. The primary and secondary pulmonary arteries were free of emboli at 7 days, but a sizeable peripheral volume of the lung at the left base remained underperfused.

CASE IV. R. P., a 54 year old Negro male, was subjected to a suprapubic cystostomy on January 4, 1968 because of prostatic obstruction, urinary incontinence and pyelonephritis. He had extensive infection of the buttocks and gangrene of the scrotum which was aggravated by his urinary incontinence. Postoperatively, he had a septicemia and evidence of thrombophlebitis in his right arm. On January 11, 1968 while sitting in a sitz bath, he had a sudden onset of dyspnea and became cyanotic with tachycardia, and the blood pressure was 70 systolic. The temperature was elevated to 103° F., and it was first thought that he was suffering from a pyemia or septicemia. The next day a lung scan showed underperfusion of both lungs. A selective pulmonary angiogram (Fig. 4*A*) showed a large thromboembolus severely obstructing the ascending right pulmonary artery and decreasing the flow to the descending pulmonary artery. An even larger embolus severely obstructed most of the major branches of the

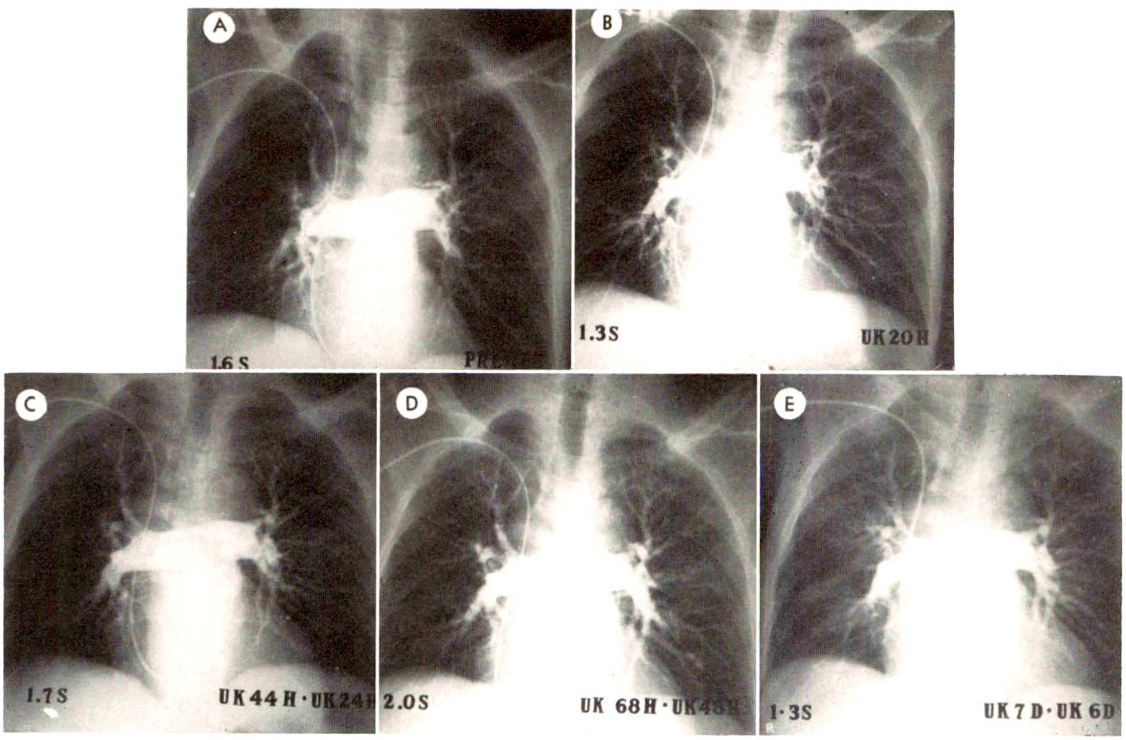


FIG. 4. Case IV. Example of good response. (*A*) Angiogram performed 36 hours after onset of symptoms. There are large emboli in both pulmonary arteries. (*B*) Angiogram 20 hours after administration of urokinase. The emboli are smaller, and perfusion of both lungs appears improved. Pulmonary artery pressure has dropped from 30 to 20 mm. Hg. A second dose of urokinase was given. (*C*) Angiogram at 44 hours. The thromboemboli are further reduced in size. (*D*) Angiogram at 68 hours. The thromboembolus in the right artery has reduced sufficiently to permit good perfusion of the upper lobe. (*E*) Angiogram at 7 days. Only very small remnants of the large central emboli can be seen.

left pulmonary artery. Pulmonary blood flow was estimated to be reduced by more than 50 per cent. The pulmonary artery pressure, pulmonary resistance and cardiac output were all abnormal (Fig. 7). A dose of 710,000 units of urokinase was given over a period of 10 minutes into the main pulmonary artery. A second angiogram 20 hours after administration of urokinase showed a diminution in size of the emboli in each artery with improved peripheral perfusion (Fig. 4*B*). The pulmonary artery pressure and pulmonary resistance decreased significantly. A second dose of 750,000 units was given and a further decrease in the size of the emboli occurred (Fig. 4*C*). By the third day only a small residual embolus remained in the left upper lobar artery (Fig. 4*D*). Scanning at this time showed underperfusion in the periphery of the right lung. On the 7th day, an angiogram showed complete clearing of the central emboli, although the right mid lung field was underperfused (Fig. 4*E*). The scan was normal.

The patient improved, but later he began again with a septic course and succumbed about 5 months later due to extensive pyelonephritis and a large perinephric abscess. At postmortem examination, a careful study of the pulmonary artery showed no residual evidence of pulmonary thromboemboli.

Comment. The response here was quite satisfactory, and all the large central emboli cleared in 7 days. There was some discrepancy between the pulmonary scan and the angiogram which is yet unexplained.

EXAMPLE OF PARTIAL OR INCOMPLETE RESPONSE

Case v. E. P., a 55 year old Negro male, was admitted to the hospital on December 3, 1967 with a complaint of dull aching pain in the lower chest of 7 days' duration.

The patient had suffered a fracture of his left tibia and fibula on November 1, 1967 and the lower leg had been placed in a cast. The patient was discharged on November 18, 1967. On November 27, 1967 he began to have a dull aching pain in the left lower chest. This was associated with some shortness of breath and thick sputum but no hemoptysis. Shortly after admission, the patient had a sudden onset of left lower chest pain. Since the patient had a sickle cell trait, the possibility of a splenic infarction was considered. The possibility of a pulmonary embolus was suggested by the surgical consultant, and a pulmonary angiogram was obtained on December 5, 1967 (Fig. 5*A*). A large thromboembolus was seen in the right main pulmonary artery partially obstructing the upper lobe branches, with underperfusion of the upper and middle lobes. On the left side, 2 sizeable thromboemboli were seen in the main pulmonary artery, and these obstructed the upper lobe and decreased the flow to the lower lobe. Urokinase in a dosage of 1,500,000 units was given into the main pulmonary artery. A second angiogram at 24 hours showed that the thromboembolus in the right pulmonary artery was less distinct and smaller, and that the upper lobe perfusion was improved (Fig. 5*B*). On the left side, the 2 central thromboemboli were considerably smaller, but the left upper lobe was almost bloodless. A second dose of urokinase, 840,000 units, was given into the main pulmonary artery. Twenty-four hours later and 48 hours after the beginning of urokinase treatment, the large thromboembolus in the right artery had decreased only slightly, but there was continued improvement in the perfusion of the right lung (Fig. 5*C*). On the left side, the upper lobe remained underperfused, although the large central emboli were scarcely visible. During the ensuing 4 days, the vascular system of the left lung returned to normal except for slight underperfusion at the left base (Fig. 5*D*). The large embolus in the right artery continued to obstruct the upper lobe artery, although it had decreased slowly in size over the 7 day period (Fig. 5*E*). During the same period, the patient had continued to improve, although he had an intermittent elevation of temperature, the cause of which is not explained. At the time of discharge from the hospital, the patient was still short of breath, although this had improved considerably. The patient was seen again on December 13, 1967 when it was recorded that he had had a bronchitis but was generally improved.

Comment. The onset of symptoms of pulmonary thromboembolism was not as certain or definite as in the cases previously presented. The first embolization could have occurred a week or more preceding the use of urokinase. The last episode was definite enough to excite suspicion and lead to a diagnosis. The patient's symptomatic response likewise was not as definite or satis-

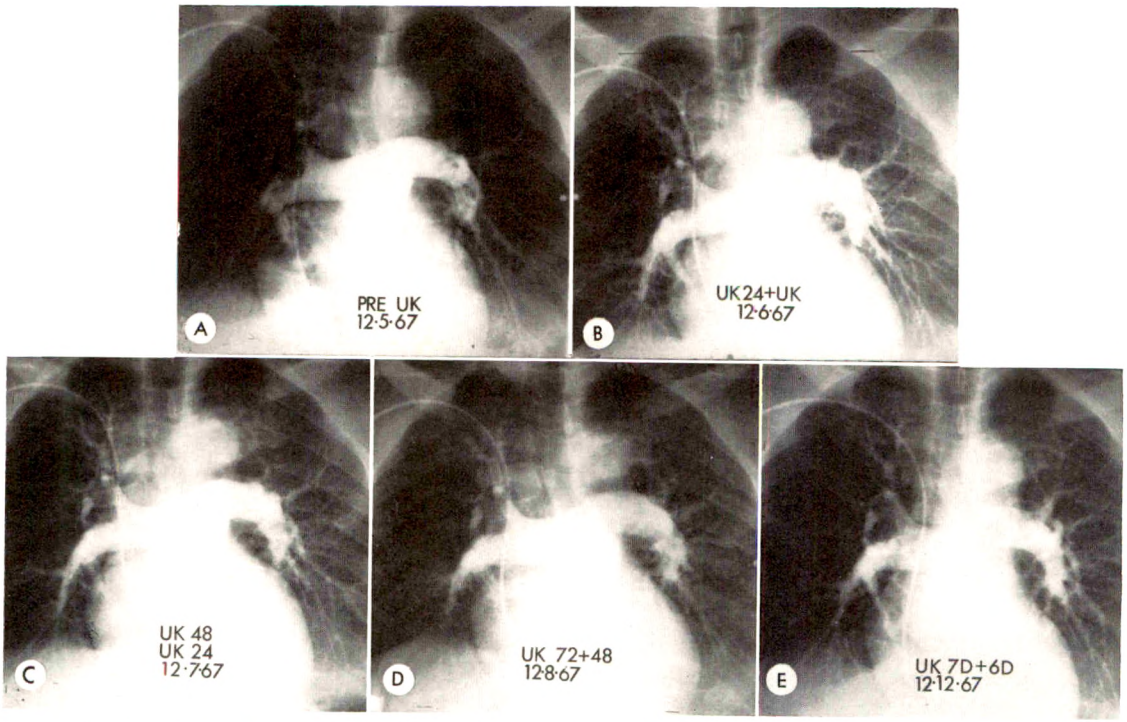


FIG. 5. Case v. Example of partial or incomplete response. (*A*) Pretreatment angiogram. (*B*, *C*, *D* and *E*) Angiograms at 24, 48, 72 hours and 7 days (see text). The large saddle-shaped embolus in the right artery persisted over the 7 day period of observation but became progressively smaller. The irregular-shaped embolus in the left pulmonary artery disappeared, but the smaller branches were attenuated, and perfusion of the left lung was diminished.

factory as that observed in the previously described cases. The hemodynamic data suggest, however, that there was no significant obstruction of the vascular system at the end of the period of observation. The large embolus in the right pulmonary artery, however, remained visible at the end of 7 days, and there was underperfusion at the left base. It is quite possible that the embolus in the right pulmonary artery was older than those in the left pulmonary artery which responded more rapidly.

EXAMPLE OF MINIMAL RESPONSE

CASE VI. F. B., a 38 year old Negro male, was admitted on February 16, 1968 for an attempt to convert atrial fibrillation to a normal rhythm. This patient had had an acute myocardial infarction 4 years previously, and this was followed by congestive heart failure and atrial fibrillation. At the time of admission, the patient was complaining of shortness of breath. The heart was markedly enlarged, the lungs were congested, and there was a small amount of fluid in each pleural space. On the night of admission, the patient complained of substernal pain and heavy sweating, and this was not relieved by nitroglycerin. On the 3rd hospital day, there was hemoptysis, and a lung scan showed no perfusion in the left lower lung and underperfusion of the right lower lung. A catheter was placed in the main pulmonary artery, and the mean pressure was 46 mm. Hg. The pulmonary angiogram (Fig. 6*A*) showed an eccentric partial occlusion of the descending branch of the right pulmonary artery with some underperfusion of the lower lung. On the left side, a massive thromboembolus occluded all of the left pulmonary artery except 2 small branches to the upper lobe. There was extensive peripheral underperfusion. A dose of 1,260,000 units of urokinase was administered through the catheter. An angiogram 20 hours later (Fig. 6*B*) showed a slight increase in the size of the descending branch of the right pulmonary artery, but the left was unchanged. At this time, the patient was given an additional 1,260,000 units

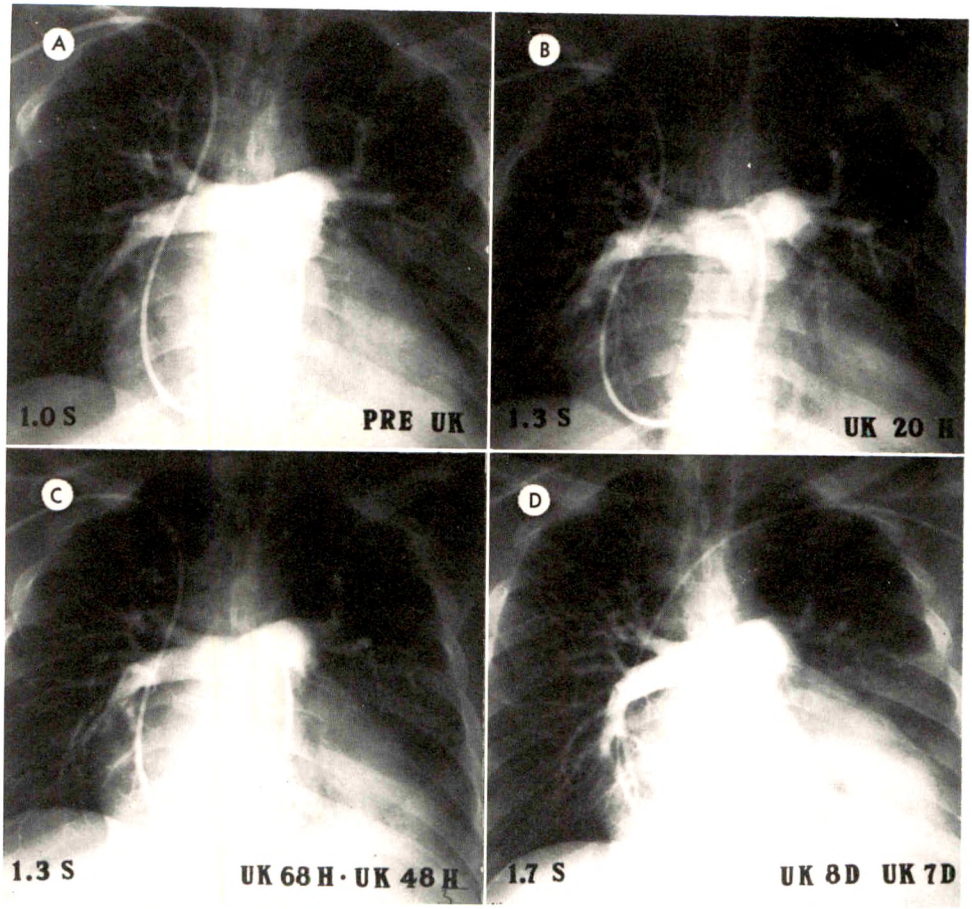


FIG. 6. Case VI. Example of no significant response. (*A*) Pretreatment angiogram performed 3 days after onset of acute symptoms. The patient had a 4 year history of intermittent heart failure. (*B*, *C* and *D*) Angiograms at 20, 68 hours and 8 days following administration of urokinase (see text). The right lower lobe artery opened but the lateral basilar branch was still completely obstructed at 8 days. The massive embolus in the left artery remained unchanged during the period of observation.

of urokinase. An angiogram 68 hours after the first dose of urokinase and 48 hours after the second showed some improvement of perfusion in the right lung but no change in the left lung (Fig. 6*C*). At 8 days, the perfusion of the right lung was approaching the normal, although one of the smaller branches was truncated (Fig. 6*D*). The left remained unchanged. The pulmonary artery mean pressure after a slight decline stabilized at about 40 mm. Hg. The patient made a slow recovery, part of which was due to the control of his heart failure. A follow-up examination after 4 months showed no further evidence of pulmonary thromboembolism.

Comment. It is well known that chronic passive congestion of the lung predisposes to pulmonary infarction. The question could be posed if congestion has anything to do with the speed and degree of resolution of large thromboemboli. The history of this patient is compatible with the occurrence of repeated emboli over a period of several years since his myocardial infarction in 1964. It could be postulated that the present episode may have been due to an additional small embolus to the right descending branch of the pulmonary artery. This fresh embolization responded to urokinase, whereas the massive obstruction of the left artery was due to old thromboemboli which had failed to resolve and were perhaps undergoing organization: this would

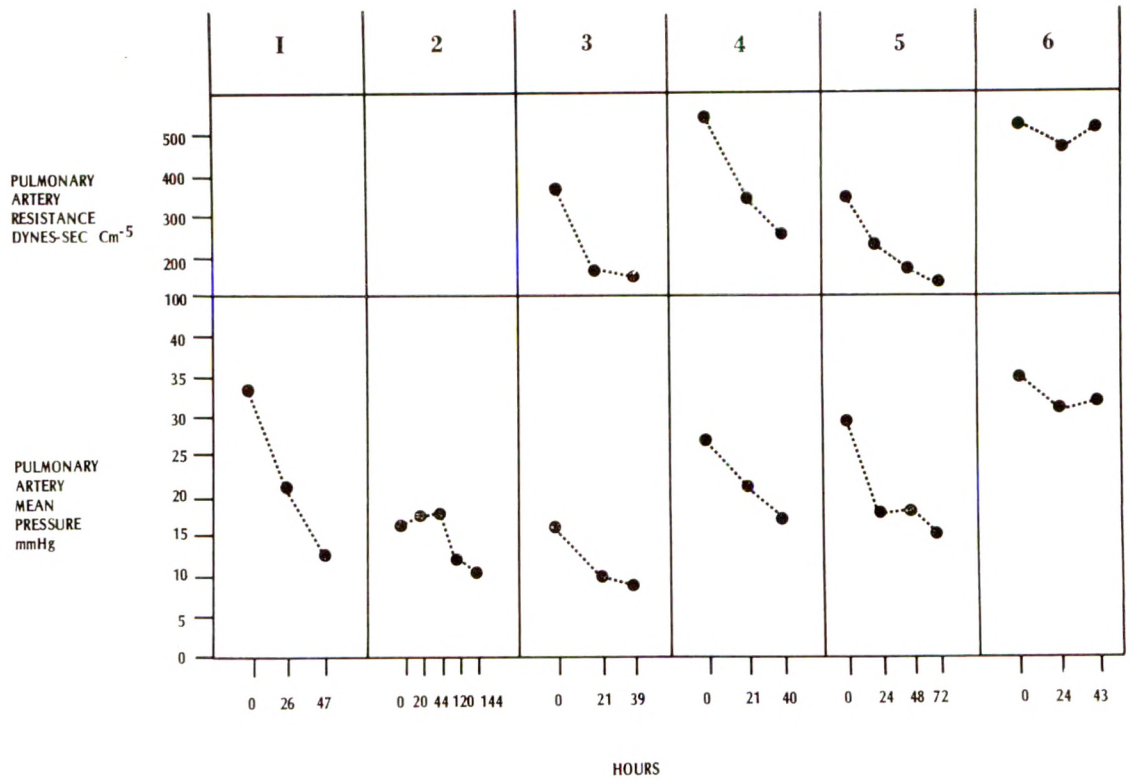


FIG. 7. Hemodynamic data from the 6 patients described in the text. In Case II there was evidence of continued embolization during the first 72 hours of treatment. In Case VI there was slight angiographic evidence of response to urokinase.

lead to a permanent obstruction. Even a relatively small pulmonary embolus in the future could produce serious disturbance or death in this patient.

DISCUSSION

The striking decrease and disappearance of massive and evidently quite recent pulmonary thromboemboli in Cases I, II, III and IV suggest that urokinase activated a strong fibrinolytic response. It is also tempting to explain the significant but lesser changes in Cases V, VII and VIII to a response to urokinase of emboli of varying ages. A number of observations[4,6,10,12] suggest that even large emboli decrease significantly in size in 4 to 7 days with a corresponding improvement in pulmonary perfusion. The data of Tow and Wagner[12] suggest that little change in lung perfusion can be expected in less than 4 days, and in massive embolization, little improvement can be expected before the 8th day. However, in the angiographic observations reported by Sautter *et al.*[9] and Sasahara *et al.*[8] and in our own cases, striking improvement occurred within hours after the administration of urokinase. However, the question does remain as to whether fresh massive emboli in the pulmonary arteries can be expected to resolve spontaneously or with heparin therapy alone in 4 to 5 days in a significant number of cases. In other words, we need an adequate control group of cases of massive pulmonary thromboembolism for comparison.

The second aspect of the disappearance of pulmonary thromboemboli revolves around an evaluation of how much of the disintegration of the thromboembolus is due to lysis and how much to fragmentation. On the 2nd and 3rd day after treat-

ment, the large central mass in a number of instances was markedly decreased in size, but emboli 5 mm. or less in diameter had appeared in the mid lung fields. At 7 to 9 days, certain peripheral segments still appeared underperfused, although this was difficult to judge. These findings appear to be corroborated by several lung scans which showed crescentic peripheral areas of underperfusion. Also, since our scans were taken in only 1 projection, significant underperfusion may have been missed.

Assuming that some of the disintegration of the thromboembolus was due to fragmentation, what were the possible effects? Our hemodynamic data indicate that if fragmentation occurs it does not sufficiently obstruct the pulmonary vascular system. As the large central mass decreased in size, the pulmonary flow increased, and the pulmonary resistance dropped. Consequently, whereas the smaller fragments may have obstructed, they were not a significant factor. Whether these smaller fragments are lysed further or whether they organize and permanently narrow or obliterate the smaller peripheral arteries is undetermined. In the single case in our series that came to autopsy nearly 6 months after massive embolization, the arterial system, including the small arteries and arterioles, was entirely normal (Case IV).

To answer these questions and further confirm our observations, we need a much larger experience. Also, as indicated above, we need angiographic, hemodynamic and scan observations on a group of control patients treated only with heparin or other anticoagulants. Only then can we properly assess the contributions of the use of urokinase. Nevertheless, the impression remains that urokinase has great promise in the treatment of massive and fresh pulmonary emboli.

The complications of treatment were minor. In 2 cases, a second episode of embolization occurred within 48 hours of the initiation of treatment. Urokinase could lyse enough of the exterior of a thrombus to result in dislodgement. Whether this will constitute an additional hazard remains to be determined.

Bleeding at the site of catheter insertion in 1 case was easily controlled. Although we have found that the extremely rapid instillation of urokinase may be followed by a momentary drop in peripheral blood pressure,[3] this can be avoided by a slower infusion over a period of 6 to 10 minutes.

In those cases (Cases VI and X) in which minimal change occurred in the visible emboli, the probability that we were dealing with old emboli is quite likely. However, in Case VI, the most recent episode began only 3 days before treatment. In this case there was an added factor, namely chronic left ventricular failure. We know that infarctions are much more common when left ventricular failure is present, and it may well be that spontaneous lysis is much less likely in the presence of chronic passive congestion of the lungs. It could be that a mechanical effect associated with a decreased pulmonary blood flow may result in both an increased time for lysis and a lack of fragmentation of the embolus. We agree with the opinion of Sautter *et al.*[9] that urokinase will be effective only in those emboli in which lysis would have occurred spontaneously. It is probable that lysis is much less common in the lung with chronic passive congestion.

SUMMARY

Urokinase, an activator of the proenzyme of the fibrinolytic system, has been injected by catheter into the pulmonary circulation in a single dose of 15,000 CTA units per kg. of body weight in the treatment of 10 patients with recent, and in most cases, massive pulmonary thromboembolism. Other investigators in most instances have used about 2.5 times as much urokinase per patient administered through a continuous intravenous infusion over an 8 hour period.

The evolution of the thromboemboli was followed by serial angiograms at daily intervals for 2 to 3 days and again at 6 to 9 days, by monitoring of the pulmonary arterial pressures, flows and resistances, the

clinical course, and, in most instances, lung scans.

The results were classified as good to excellent in 4 cases, partial or incomplete in 4, and minimal in 1. Observations in 1 patient were incomplete.

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RAPID BLOOD FLOW RATE ANALYSIS DURING ROUTINE SELECTIVE ARTERIOGRAPHY: AN APPLICATION OF TELEVISION FLUORODENSITOMETRY*

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THE clinical measurement of human arterial blood flow rates has been difficult and only moderately accurate in most areas. In several vital areas, rates of flow have been impossible to obtain. Utilizing a new system for converting the optical fluoroscopic image into an electronic signal and using simple opaque medium dilution theory, acceptably accurate blood flow rates can be determined in any artery suitable for selective catheterization. The technique requires little additional equipment not already available in most diagnostic radiology departments.

MATERIALS AND METHODS

The television monitored image amplified fluoroscope which is routinely used for catheter positioning during arteriography was modified so that the video signal and the vertical video synchronization pulse can be easily coupled to an oscilloscope. Since the television picture is made up of a series of horizontal lines (rasters) which are framed at a rapid rate, the fluoroscopic image can be directly related, point by point, to corresponding segments of the television image. Utilizing the variable time delay feature available in the oscilloscope, any single horizontal raster line can be sampled from the complete video picture frame. The vertical video synchronization pulse is used to trigger the sweep generator in the oscilloscope, while the video signal is used to drive the vertical deflection amplifier in a standard Techtronix No. 549 oscilloscope. This is a modification of a technique originally described by Bloch[1,2] for analysis of the image of a simple light microscope.

The conversion of the optical fluoroscopic image into an electronic signal which is proportional to the radiographic density of the subject, permits electronic densitometric sampling which is not otherwise possible.

Figure 1*A* is a cross-sectional view of a television tube on which is shown the fluoroscopic image of a tubular bone. In the plane of a single horizontal line (A), the density of electrons as they pass from the electron gun to the tube face is graphically depicted by the heavy dark line (A^1). Since the light and dark portions of the television image correspond to the electron density from the electron gun, one would expect the curve to show most absorption in the cortical areas and less in the medullary canal. In Figure 1*B*, the graph of the density (A^1) has been rotated 90° to place it in a more conventional position for analysis. The graphic form represents not only the electron density in the television tube but is directly related to the radiographic density of the object being examined by the fluoroscope.

By removing a single horizontal raster line and displaying it as a plot of time *versus* density on the face of the oscilloscope, a curve representing the radiographic density of the subject at the line location is obtained. This is demonstrated in the composite Figure 2 in which the fluoroscopic image of a femur is seen in the

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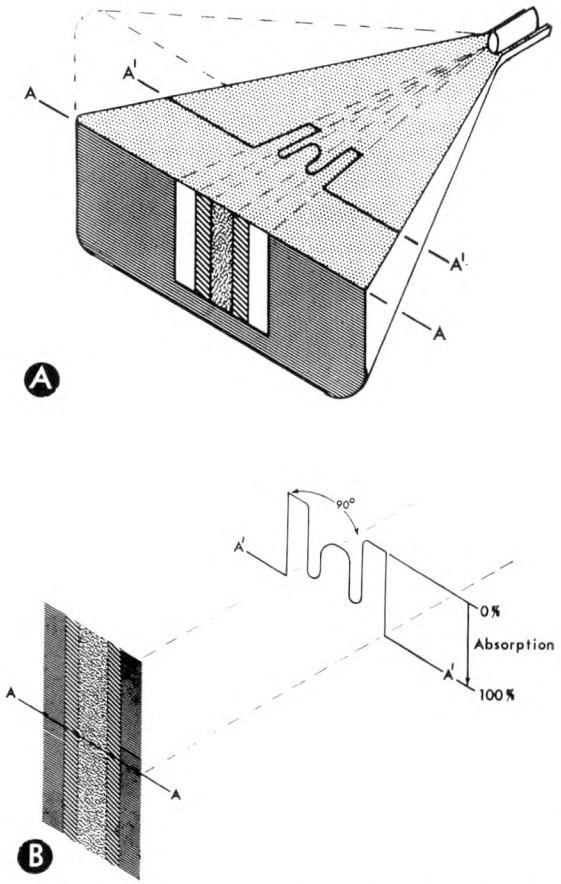


Fig. 1. (*A*) A cross-section illustration of a television tube shows the fluoroscopic image of a tubular bone on the face of the tube. In the plane of a single horizontal line (A), the density of electrons as they pass from the electron gun to the tube face is graphically shown (A^1). The shading of the television image corresponds to the fluoroscopic image which, in turn, is the result of the radiographic density of the subject. As expected, more x-ray absorption occurs in the cortex of the bone than in the medullary canal, and the curve (A^1) would be the expected result. Thus, the optical image has been converted to an electronic signal suitable for rapid analysis. (*B*) The graph of the density (A^1) has been rotated 90° to place it in a more conventional position for analysis.

upper portion (Fig. 2*A*), and the resultant densitometric curve is seen in the lower portion (Fig. 2*B*). It should be noted that the single line being sampled is automatically removed from the video frame and, therefore, appears on the television screen as a bright white line (Fig. 2*A*). This feature provides accurate positioning information as to the area from which the sample is

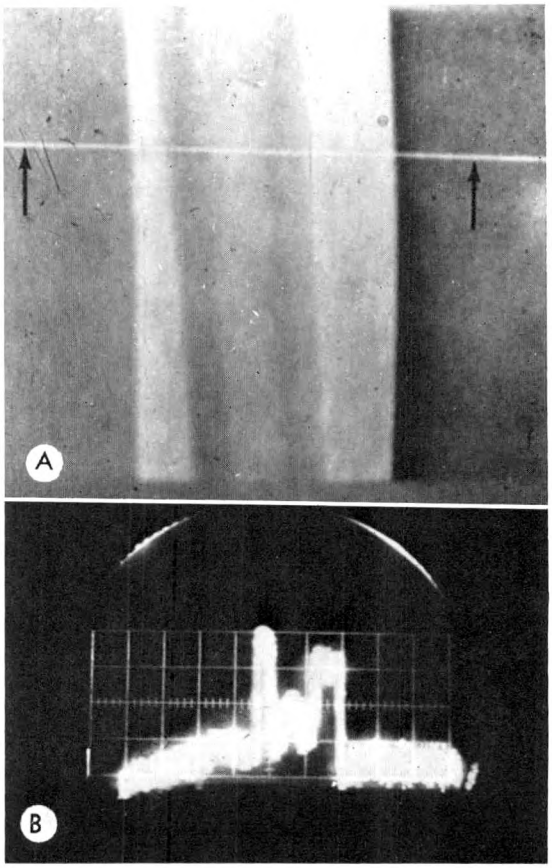


Fig. 2. (*A*) A photograph of a television monitor on which is seen the fluoroscopic image of a normal femur. The bright white line traversing the television screen (vertical arrows) is created by the removal of this voltage from the composite video signal for densitometric analysis. (*B*) The oscilloscope records the voltage obtained from the above line and the resultant curve conforms to the theoretical curve shown in Figure 1.

being obtained. Analysis of multiple subjects has shown that the television monitor can be used as a densitometer and it is this technique which we have described as television fluorodensitometry. A detailed paper on the technical aspects of this technique will be presented at a later date.

$$\text{FLOW (ml./min.)} = \text{RATE OF INJECTION OF THE OPAQUE (ml./min.)} \times \frac{\text{PERCENT CONCENTRATION OF INJECTED MATERIAL}}{\text{PERCENT CONCENTRATION OF OPAQUE IN THE ARTERY } (C_a)}$$

Fig. 3. The general formula describing the relationship of flow measurement to the dilution of an indicator material. (After S. K. Hilal, Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1966, *96*, 899.)

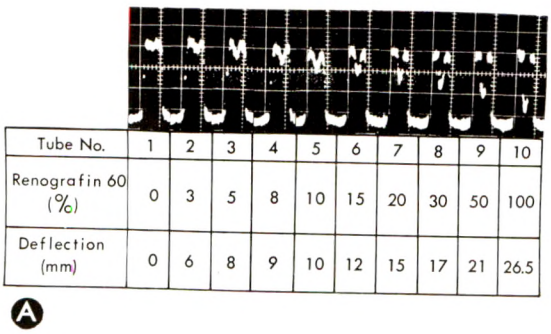
$$(A.F.) = \frac{I}{I_o} = \frac{E}{E_o} = \frac{\text{Log}_e\left(1 - \frac{D+n}{D\infty}\right)}{\text{Log}_e\left(1 - \frac{D_o+n}{D\infty}\right)}$$

$$(1)\ \text{Log}_e(A.F.) = -M C_T d_T = -M C_a d_a$$

$$(2)\ \therefore\ C_a = \frac{C_T d_T}{D_a}$$

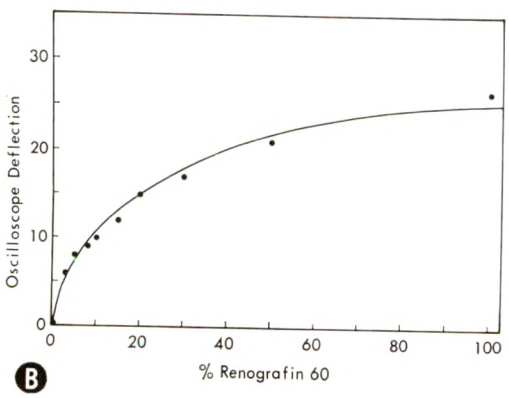
FIG. 4. Formulae used by Hilal for computing the dilution of radiographic contrast material in the vessel under study. C_a = concentration of indicator in artery; C_t = concentration derived from standard; d_a = diameter of the artery; d_t = diameter of the standard tube; A.F. = attenuation factor.

The relationship between the dilution of an indicator substance and the flow in a fluid system can be described by the Hamilton-Stewart formula.[3,5,8] Other investigators have suggested that radiographic contrast material can be used as an indicator substance and blood flow can, therefore, be computed using a tedious manual densitometric sampling technique.[3,4,6,7,9,10] Figures 3 and 4 are the formulae used for calculations by one author.[4] Utilizing similar concepts, we have



Tube No.	1	2	3	4	5	6	7	8	9	10
Renografin 60 (%)	0	3	5	8	10	15	20	30	50	100
Deflection (mm)	0	6	8	9	10	12	15	17	21	26.5

A



B

FIG. 5. (*A*) Densitometric curves obtained from the plastic phantom. The concentrations of renografin 60 per cent and the amplitude of the curves are given in the accompanying chart. (*B*) The graphic results of the data given in *A*.

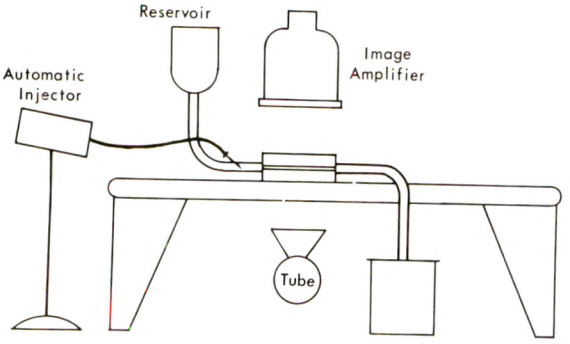
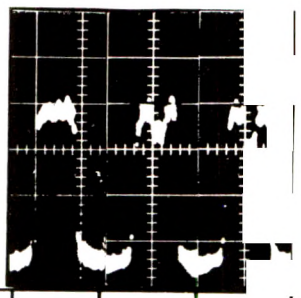


FIG. 6. An illustration of the flow block experiments. The rate of flow through the plastic block was obtained directly by measuring the time required to pass a known volume of water through the system.



Curve	A	B	C
Rate of Contrast inj. (c.c./sec)	0	10	16
Deflection (mm)	0	9	11
Renografin 60 (Calculated %)	0	8	12.5
Calculated Flow Rate (c.c./sec)	—	127	146
Actual Measured Flow Rate (c.c./sec)	167	167	167
% Error	—	13.1	11.1

FIG. 7. Representative results of a flow block experiment.

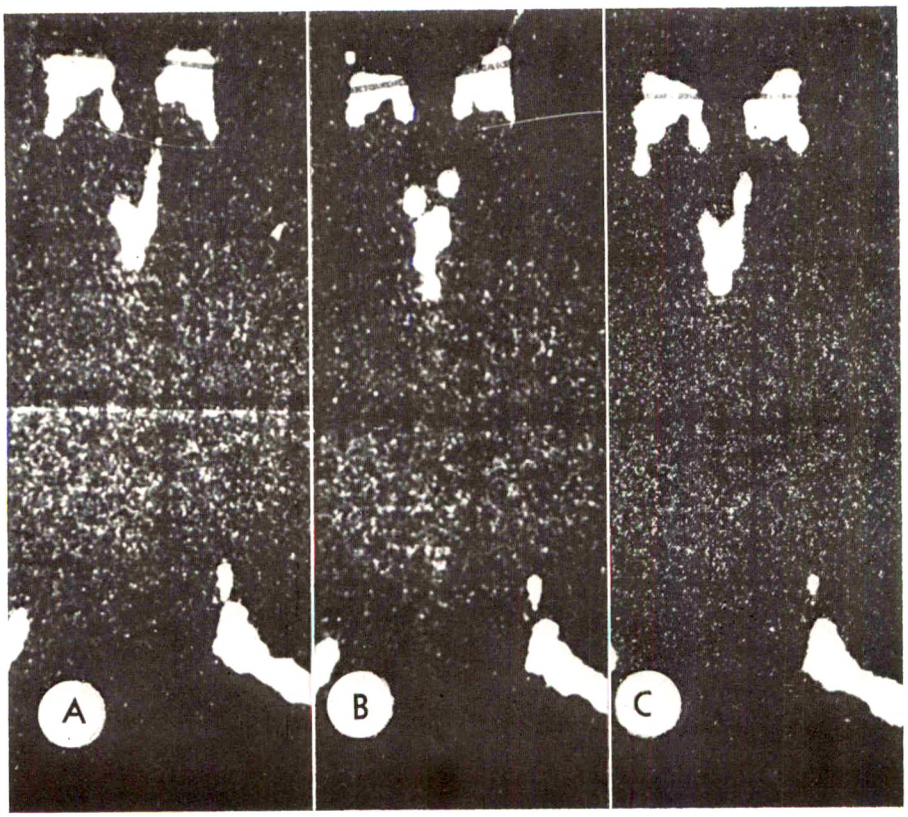


FIG. 8. (*A*, *B* and *C*) Curves demonstrating the reproducibility of the measurements in the flow block experiments. The measured flow was identical on each run and the amplitude of the density curves measures 11.5 mm., 12.0 mm., and 12.5 mm.

performed flow measurement experiments utilizing a television system as a densitometer during both *in vitro* and *in vivo* tests.

A plastic phantom was constructed with 10 parallel channels. These channels were filled with varying known concentrations of renografin 60 per cent. The resultant television densitometric curves are demonstrated in Figure 5*A*. Figure 5*B* is a graph of these results. Plastic flow blocks were also constructed with lumens of varying diameters. A flow system was set up as illustrated in Figure 6, and the flow of water through these flow blocks was determined by direct measurement. A representative sample is presented in Figure 7. The curves in Figure 8, *A*, *B* and *C* demonstrate the ability of the system to reproduce results in 3 successive measurements at the same flow rate. An *in vivo* study is demonstrated in Figure 9 during which television flow measurements were made in the femoral artery of a dog while simultaneous recordings of the flows were obtained with an electromagnetic flow meter. For our experiments, arteriotomies in the dogs' vessels provided the entryway for a tip occluded multi-side hole catheter which ensures the turbulent flow that is required for accurate measurement. Throughout the studies, no other changes were made in the routine arteriographic technique or in the clinical instrumentation utilized by our department. The results of a representative experiment are seen in Figure 10.

DISCUSSION

In order to meet the criteria of the Hamilton-Stewart formula, one needs to know: (1) the per cent concentration of the indicator substance prior to injection; (2) the rate of injection of contrast material; and (3) the final diluted concentration in the vessel of interest.[3,5,8] The first require-

ment is routinely met. The rate of injection with most commercially available automatic injectors is sufficiently accurate at low flow rates to satisfy the second requirement. Measurement of the final dilution presents a major difficulty. For adequate dilution, turbulent flow must be established.[5,8] Since the flow will be directly related to the cross-sectional area of the artery, its dimensions must be obtainable and any magnification due to fluoroscopic technique must be considered. Hilal and others have suggested that these criteria may be met utilizing a roentgenogram and



Fig. 9. A photograph of a television monitor demonstrating opacification of a dog's femoral artery. The electromagnetic square wave flow meter probe is seen in the upper portion of the picture. This vessel measured 6 mm. in diameter and a 15 mm. probe was used for the measurements.

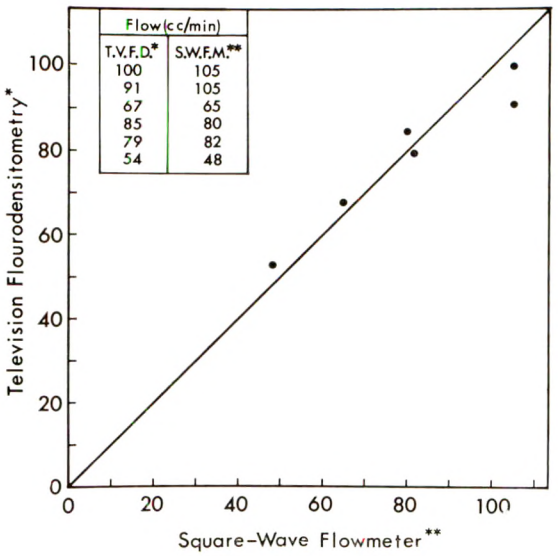


Fig. 10. The graph and chart demonstrate the results of a representative experiment. These are the values obtained from the femoral artery seen in Figure 9. From results such as these, accuracy on the order of 10–15 per cent can be expected.

standard system of densitometry.[3,4,6] Other authors have postulated that a television system could be used as a densitometer in cardiovascular analysis.[7,9,10] Utilizing a television system for the sampling device eliminates many of the problems inherent in the radiographic techniques, but at the same time introduces new problems. Radiographic factors are limited by the operational capacity of the image amplifier and of the television system to which it is coupled. In our work, no attempt was made to specifically engineer distortion or noise levels out of the television system since the primary prerequisite was that of developing a technique which utilizes standard clinical equipment which is available in most radiology departments. Fortunately, most of the errors which are related to the television system are present throughout the examination. Since only a comparison between a standard and the vessel is needed, television errors probably do not contribute significantly in the calculation if careful technique is used. The selective catheterization of the vessels of interest is done in a routine manner with a small

catheter. This, coupled with slow injection rates of contrast material minimizes changes in the normal hemodynamic pattern. The site of sampling must be within the area of turbulent flow created by the injection. While the vascular dynamics cannot be normal during the injection phase, the resultant flow rates represent a good approximation of the normal situation. It is thought that an error as great as 20 per cent would be clinically acceptable if the data were reproducible. From our experiments to date, it would appear that an error less than 20 per cent can be expected.

Since the optical information is converted to an analogue voltage, it is, therefore, immediately available for both magnetic tape recording and for high speed computer analysis. We are now developing a computer program to analyze the information obtained on-line from the subject and continuous computations of the blood flow will be available from this. Both our technique and those using a two point densitometric comparison could utilize television densitometry for analysis.

The system described above represents the first step in the development of a routine method for the clinical determination of intra-arterial blood flow. It requires little additional equipment other than that found in most diagnostic radiology departments and the techniques of arterial visualization need not be modified for its use.

SUMMARY

A new technique utilizing the television monitored image amplified fluoroscopic image for densitometric evaluation and blood flow analysis is described.

Using the television system as a sampling device, the dilution of radiographic contrast material following injection can be computed and the flow rate within the vessel determined. Accuracy of the order of 10–15 per cent can be expected.

The measurement requires no change in the techniques of the arterial visualization utilized by most departments.

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A NEW METHOD FOR CARDIAC PACEMAKER INSERTION*

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ELECTRIC stimulation by transvenous pacemaker catheters has become an accepted and indeed, in many centers, the preferred method of treatment for the Stokes-Adams syndrome, complete heart block with congestive failure, cardiac arrest, and ventricular tachycardia with or without organic heart disease.[1,4,6,8,9,10] In many instances, placement of a catheter electrode is lifesaving and must be performed as expeditiously as possible. The jugular veins have been popularized as the sites of entry because they allow easy manipulation in placing the catheter tip in its proper intracardiac position and, more important, because the neck is a relatively immobile structure: there is less chance of dislodging the pacemaker once it has been placed. The pacemaker is usually inserted by the cut-down method. The purpose of this paper is to present a simple rapid nonsurgical technique of inserting the transvenous pacemaker catheter by utilizing a percutaneous approach to the internal jugular vein.

BACKGROUND

A percutaneous method utilizing a teflon coated platinum-tipped stainless steel wire has been described previously.[3,7] This involves venipuncture of an antecubital vein with a Rochester type plastic needle. Aside from losing the previously mentioned advantages of a jugular route, problems that have occurred with this method include: (1) Difficulty in threading the catheter over the shoulder if a good basilic vein is not found; (2) inability to enter the heart or to maintain ventricular capture by the pacemaker wire because of its great flexibility; and (3) formation of a knot in the wire impeding its withdrawal. A further problem, not mentioned in previous reports, is the difficulty of finding a venipuncture site in the antecubital fossa in a critically ill patient.

The internal jugular vein has been used as a route for catheters both in the study of the intracranial venous system[2] and for pulmonary angiography.[5]

The ability to insert a closed-end catheter (which is in essence what the pacemaker catheter is) percutaneously is possible by use of a commercially available teflon introducing sheath.*

TECHNIQUE

A thin-wall 18 gauge, $4\frac{3}{4}$ inch needle is used for the jugular puncture and a flexible tipped guide wire (outer diameter 0.035 inch) is passed through the needle. A short tapered open-end introducing catheter (of the same diameter as the pacing catheter) is used to insert a tapered thin-walled sheath which fits over the catheter. This catheter and sheath are commercially available as a packaged item.* A bipolar pacemaker (French No. 6 or 7 in diameter) is eventually introduced through the sheath (Fig. 1).

With the patient supine, the chin is extended and the area from the angle of the right mandible to the right clavicle is prepared and draped. The shoulders should not be elevated, since venous pressure will drop and the vein will collapse. The internal jugular vein is a large structure lying immediately lateral to the internal and common carotid arteries. The operator's finger is placed 2 fingerbreadths below the angle of the mandible and directly over the carotid pulse (Fig. 2). The skin and subcutan-

* Catheter Introducer from United States Catheter and Instrument Company.

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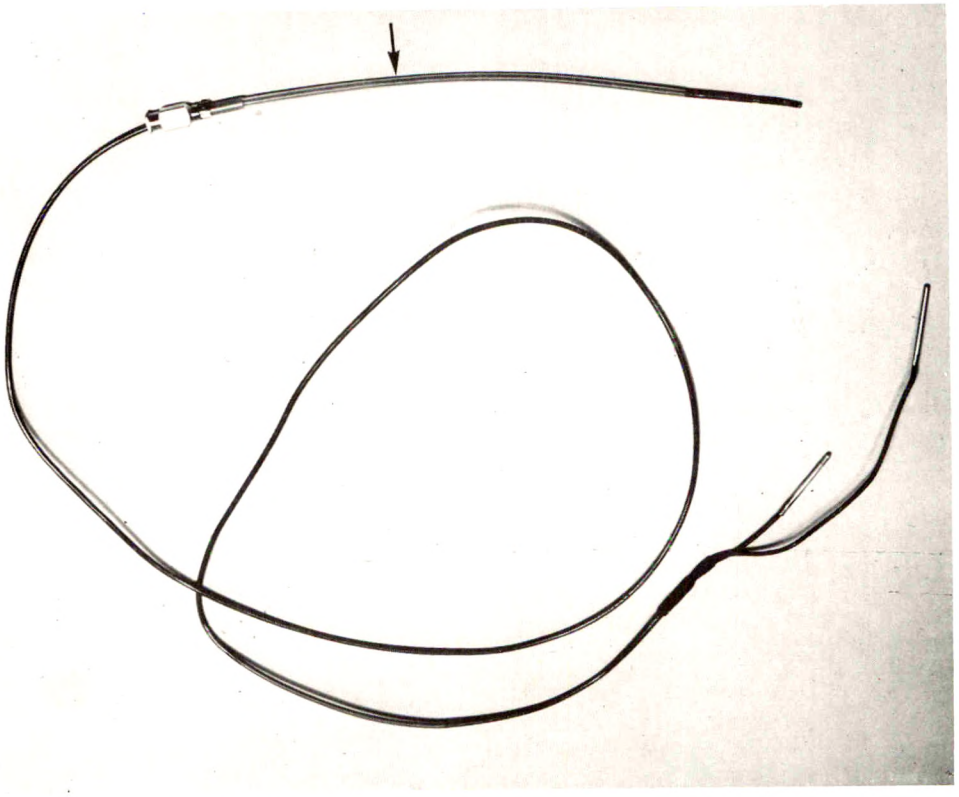


FIG. 1. Pacemaker catheter with introducing sheath (arrow) over it.

eous tissues just lateral to the pulse are infiltrated with 1 per cent Xylocaine, and a small stab wound is made in the skin to facilitate passage of the catheter and sheath. A plain tip syringe containing 5 cc. of 1 per cent Xylocaine is attached to the puncture needle. While maintaining a 45° angle with the skin, the needle is directed through the stab wound just lateral to the finger overlying the carotid pulse. Xylocaine is injected to relieve discomfort. Constant aspiration is used and a good flow of dark venous blood is seen on entrance into the internal jugular vein. A 2 or 3 cc. test injection of contrast medium will verify the needle's position if fluoroscopy is available.

Preliminary preparations are made by placing the sheath over the short open-end catheter (Fig. 3*A*). Using the Seldinger technique, the open end catheter, with the sheath over it, is threaded into the vein over the guide wire (Fig. 3*B*). The sheath is held in position and the introducing catheter is withdrawn (Fig. 3*C*). The pacemaker catheter is then inserted through the sheath into the vessel (Fig. 3*D*) and the sheath is slipped out of the skin on to the hub of the pacemaker catheter (Fig. 3*E*). The catheter is then positioned so that the tip is adjacent to the right ventricle and held until adequate pacing is obtained. The part of the catheter external to the patient is securely taped, with the battery box, to the patient's chest.

REPORT OF A CASE

C. H., a 78 year old white male, was transferred to this department from an outlying hospital. The history was obtained from the patient's relatives. He evidently was in excellent health, working as a bagger in a local grocery until 5 days prior to transfer. At that time his wife noted that he was staggering as if he were drunk, and he, himself, complained of anorexia and mild dyspnea. Two days prior to transfer he complained of intermittent upper chest pain and epigastric pain, and became

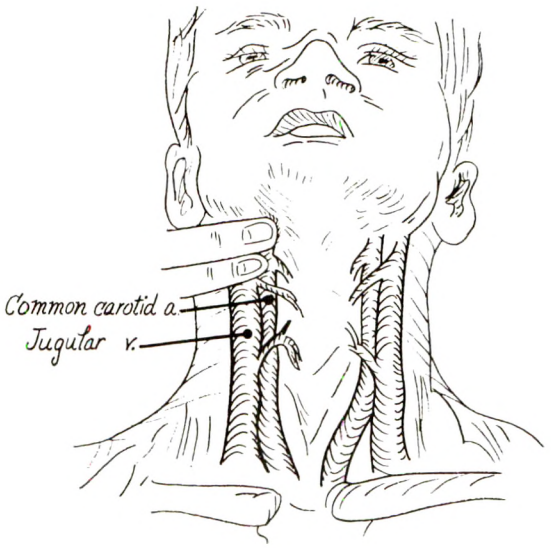


Fig. 2. Location of internal jugular vein. The needle is introduced just lateral to the carotid pulse and 2 fingerbreadths below the angle of the mandible.

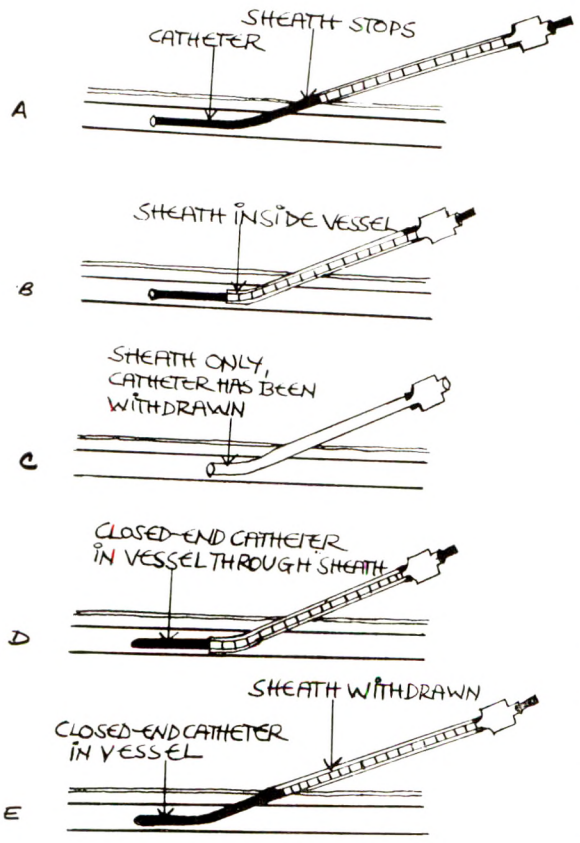


Fig. 3. (*A–E*) Steps in introducing the pacemaker catheter through the sheath.

somewhat confused. The day prior to admission he was admitted to another hospital, where the diagnosis of complete heart block was made. He was then transferred here.

On physical examination he presented as a well developed, elderly gentleman in mild respiratory distress. Blood pressure was 160/70, the pulse 30 and the respirations 20. Pertinent physical findings included Cannon waves in the neck, rales at both lung bases, a slightly enlarged heart with a cardiac rate of 30 and a varying first heart sound.

Laboratory data including blood urea nitrogen, complete blood cell count, electrolytes, and transaminase were normal.

Electrocardiography showed a bilateral bundle branch block and a complete heart block.

A chest roentgenogram revealed slight cardiomegaly and pulmonary congestion.

After 36 hours of an unsuccessful attempt at drug therapy with sublingual and intravenous isuprel, the patient was taken to the Cardiac Catheterization Laboratory where a bipolar catheter electrode was positioned, utilizing the technique described above. This catheter was left in position for 10 days, at which time a permanent thoracic pacemaker was implanted.

Two weeks following permanent pacemaker implantation the patient was transferred back to his referring hospital.

Comment. Although at the time of writing we have used this approach for catheter pacemaker placement in only the case mentioned, one of us (R.H.) has used this approach standardly in numerous cases for pulmonary angiography. There have been no technical difficulties or significant sequelae suffered by the patients.

SUMMARY

A nonsurgical percutaneous approach utilizing the internal jugular vein for insertion of a transvenous pacemaker catheter is described.

Pacing can be rapidly accomplished, since a cut-down is not necessary nor is a frantic search for the external jugular vein necessary in the critically ill patient.

It is a relatively simple technique and one that can be easily performed by any physician who has had percutaneous catheterization experience.

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INTRAPULMONARY LYMPH NODE DETECTED ROENTGENOLOGICALLY; CASE REPORT*

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REFERENCES to peripheral intrapulmonary lymph nodes are scant and many physicians are unaware of their existence. However, several examples which were demonstrated roentgenographically have been recently reported.[2,3,4,6] Recognition that such lymph nodes may be detected in normal lungs is particularly important to radiologists. To this end the following report of a subpleural lymph node presenting as a solitary pulmonary nodule on roentgenologic examination is made and previous reports in the literature are summarized.

REPORT OF CASE

Clinical Findings. A 47 year old Caucasian male had a mixed tumor of the parotid gland excised in July, 1966. A routine preoperative chest roentgenogram revealed a solitary nodule which was not evident on roentgenograms taken 3 years earlier and he was referred to The University of Michigan Medical Center for further investigation.

The patient was in good health and symptomless. A history of right-sided pneumonia on 4 previous occasions was obtained. He had smoked 1 to 2 packs of cigarettes for 20 years. Further chest roentgenograms demonstrated a faint circumscribed 1 cm. nodular density within the right lower lobe at the level of the 8th posterior intercostal space near the lateral costophrenic sulcus (Fig. 1). Laminograms showed no cavitation or calcification within the nodule (Fig. 2). Clinical investigation revealed no evidence of neoplasm or granulomatous disease. In September, 1966, a wedge resection of the posterior segment of the right lower lobe was done.

Pathologic Findings. Within the pulmonary parenchyma, just beneath the pleura, was a circumscribed, roughly spherical gray-black nodule, 1 cm. in diameter. The adjacent lung tissue was grossly normal. This nodule of

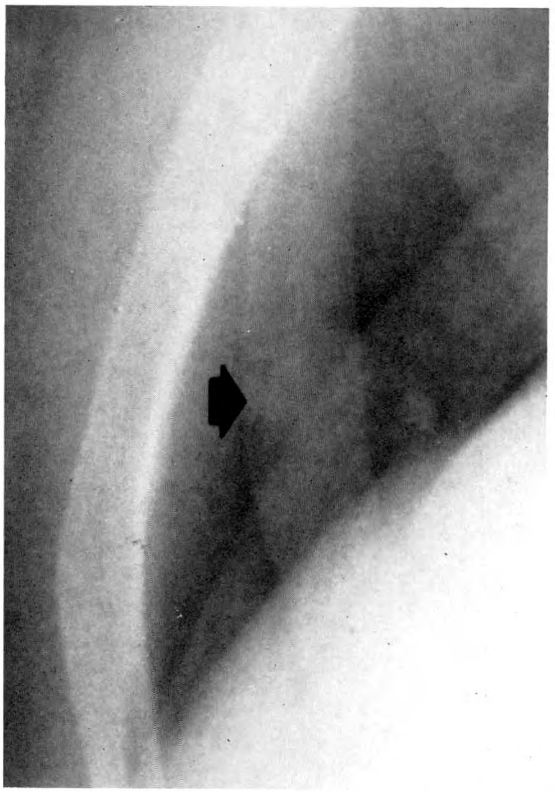


Fig. 1. A faint non-calcified nodule (arrow) 1 cm. in diameter is present in the right lower lobe. A smaller nodule, projected medial to this one, was more anterior and its nature was not verified.

lymphoreticular tissue was enclosed by a thin, well defined fibrous capsule (Fig. 3). The cortex consisted of primary lymphoid nodules with small germinal centers (Fig. 4). Hyperplastic reticuloendothelial cells, heavily laden with anthracotic pigment, comprised most of the medulla. Scattered deposits of hemosiderin were present. A definite but narrow subcapsular sinus communicated with the medulla by a coarse interfollicular mesh in which hyperplastic reticuloendothelial cells contained anthracotic pigment. There was no significant inflammation. The microscopic features were those of a normally structured lymph node

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FIG. 2. Laminogram showing the noncalcified nodule shown in Figure 1.

with reticular and endothelial hyperplasia and anthracosis.

DISCUSSION

Reports of lymph nodes within the peripheral lung in the absence of significant pulmonary disease are few. They have been demonstrated not only by histologic studies[4] but also by subpleural lymphangiography.[9] The assumption has been that these isolated lymph nodes develop from loose lymphoreticular aggregates in response to irritating dusts and noxious agents.[4] In the case presented there was less anthracosis of the adjacent lung parenchyma than is commonly seen in patients of this age with long histories of smoking, and no chronic lung disease was evident. It seems more logical to consider these lymph nodes to be of developmental origin with both afferent and efferent connections and the anthracosis to be a filtration residue. Chronic inflammation and irritation from dusts could be expected to cause hyperplasia and make a rudimentary lymph node more readily detectable. That the lesion in this case was truly a lymph node is indicated by the presence of a capsule with a subcapsular sinus, cortical lymphoid nodules with germinal centers and prominent central and interfollicular reticular mesh. It was not a lymphoid hamartoma as has been described in the hilum of the lung and mediastinum.[1]

Seven previously reported cases of pulmonary lymph nodes detected preoperatively are summarized in Table 1. All but 2 patients were males and only 2 were under 40 years of age. Most were described as moderately heavy cigarette smokers. The lymph nodes were always subpleural in location and usually described as hyperplastic and anthracotic. In 1 patient the lymph nodes were multiple.[6] All lesions detected roentgenologically were located in

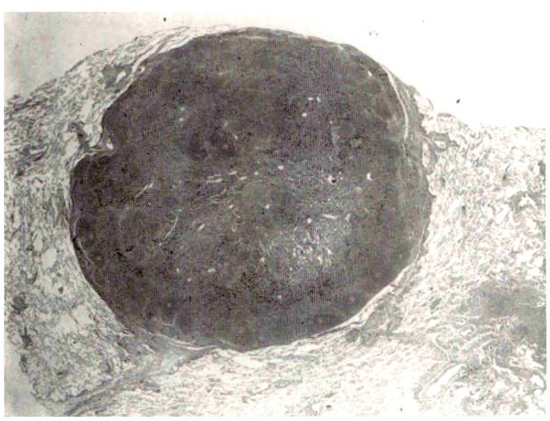


FIG. 3. Encapsulated lymph node within otherwise normal lung parenchyma (hematoxylin-eosin ×15).

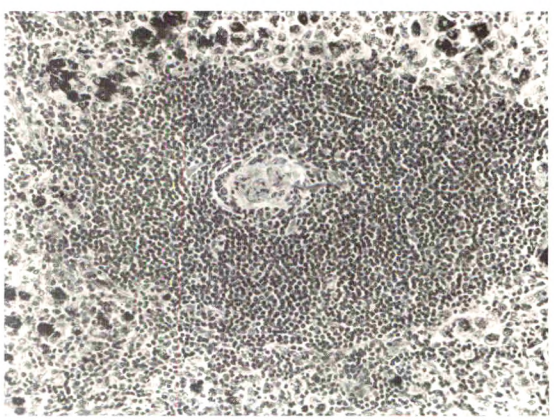


FIG. 4. Lymphoid nodule of cortex with small germinal center. The surrounding mesh has numerous large pale reticuloendothelial cells containing anthracotic pigment (hematoxylin-eosin ×195).

Table I

PREVIOUSLY REPORTED CASES OF INTRAPULMONARY LYMPH NODES

	Sex	Age	Location
Steele[8]*	M	48	Subpleural; LLL
Katz[3]	M	46	Subpleural; LLL
Greenberg[2]	M	58	Subpleural; RLL
Rosenthal and Weg[5]	M	37	Subpleural; RLL
	M	47	Subpleural; Lingula
Shapiro *et al.*[6]	F	41	Subpleural; RLL, Lingula, LLL†
	F	30	Subpleural; RLL

* Three other cases listed but not described.
† Two nodes in RLL, 2 in lingula, and 1 in LLL.
LLL = left lower lobe. RLL = right lower lobe.

the lower lobes or lingula, without a segmental preference. This distribution correlates with regions where dust particles tend to collect[7] and lends credulence to the suggestion that such particles either stimulate the formation of lymph nodes or cause inconspicuous rudimentary nodes to become hyperplastic and more readily detected. In all cases the nodes appeared on plain chest roentgenograms as rather faint, circumscribed nodules, without cavitation or calcification, and measured 0.5 to 2.0 cm. in diameter. Although they must be considered in the differential diagnosis of solitary pulmonary lesions, they are apparently very infrequent. Steele[8] in a review of 887 resected solitary pulmonary nodules in males found only 4 to be subpleural lymph nodes.

SUMMARY

An example of solitary subpleural intrapulmonary lymph node in a 47 year old man, detected roentgenologically and confirmed by histologic examination, is reported.

This lesion should be included in the differential diagnosis when a solitary nodule without calcification or cavitation is observed in the lower lung.

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The authors wish to thank Dr. Cameron Haight, M.D. for permission to publish this case.

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ROENTGEN FINDINGS IN EXTRAMEDULLARY HEMATOPOIESIS*

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EXTRAMEDULLARY hematopoiesis is a compensatory mechanism, which develops when the blood forming organs are unable to maintain a rate of erythrocyte formation sufficient for the body demand. This may occur when erythrocytes are removed too rapidly from the blood stream or when the rate of erythrocyte formation in the bone marrow is decreased. Extramedullary hematopoiesis has been described in severe anemia,[50] myelofibrosis,[12] polycythemia,[50] erythroblastosis fetalis,[10] leukemia,[43] Hodgkin's disease,[49] carcinomatosis,[27] hyperparathyroidism,[52] and rickets.[26] Most cases are associated with congenital hemolytic anemia.

There have been 2 reports[15,42] of thoracic extramedullary hematopoietic masses in patients who did not have anemia or any other chronic disease. In both, the diagnosis was made as an incidental finding at autopsy. Although the diagnosis of thoracic extramedullary hematopoiesis was considered preoperatively in only 5 of the 26 reported cases (Table 1), the condition is not as rare as this figure suggests and a confident diagnosis based on roentgenographic and clinical features can be made.

When there is a prolonged discrepancy between the supply and demand for erythrocytes, blood formation occurs in those areas where it does in the fetus, namely the liver, spleen, adrenal, heart, thymus, lungs, lymph nodes, renal pelvis, retroperitoneal fat, gastrointestinal lymphatics and dura mater.[2,7] Masses of extramedullary hematopoietic tissues have been demonstrated roentgenographically in the thorax and spinal canal.

It is the purpose of this report to present 1 case where the positive roentgenographic diagnosis of thoracic extramedullary hematopoiesis was made. The suggestion that the patient's neurologic symptoms were due to spinal extramedullary hematopoiesis led to confirmation by myelography and successful treatment with irradiation. Three other cases of extramedullary hematopoiesis with roentgenographic findings are briefly reported and a characteristic configuration of the ribs in some patients who have long-standing thalassemia is suggested.

REPORT OF CASES

CASE 1. E.R., a 23 year old white female of non-Mediterranean extraction was hospitalized for evaluation of progressive bilateral leg weakness of 1 year's duration.

When she was 6 years old, congenital hemolytic anemia, probably thalassemia intermedia, was diagnosed. Both parents and a sibling were hematologically normal. Her hematocrit was 28 per cent and she received several elective transfusions at that time, but has received none since. Although her hematocrit remained about 25 per cent and she had occasional jaundice, she developed normally and remained well until 2 years ago, when she developed mild low back pain, pedal edema, a chronic ulcer of the left ankle, and later, bilateral leg weakness.

On physical examination she was noted to be alert, well developed and mildly jaundiced with a 3 cm. ulcer over the left medial malleolus and mild left pedal edema. Frontal bossing of the head was present, over which a bruit was heard. The liver was palpated 3 cm., and the spleen 5 cm. below the costochondral margin. She had weakness of the calf and thigh muscles bilaterally, poor position sense of the toes, a broad based gait and a positive Romberg's sign. The deep tendon reflexes were hyperactive with unsustained clonus, and bilateral Babinski's signs were present. Pinprick sensation was diminished up to the eighth thoracic nerve level. The remainder of the neurologic examination was normal.

The chest roentgenograms showed a large lobulated paraspinal soft tissue mass (Fig. 1, *A*

* From the Department of Radiology, Strong Memorial Hospital, Rochester, New York.

TABLE I

REPORTED CASES OF THORACIC EXTRAMEDULLARY HEMATOPOIESIS

Date of Report	Author	Primary Disease	Age (yr.)	Sex	Site
1925	Saleeby[42]	Bronchopneumonia	81	F	T 5 bilateral
		Osteitis fibrosa cystica	21	F	Unilateral
1927	Brannan[2]	Erythroblastic anemia	7½ mo.	M	Posterior and anterior mediastinal lymph nodes
1930	Plonskier[41]	Carcinoma of stomach	70	F	T 6–T 10 bilateral
1931	Dawson[11]	Hereditary spherocytosis	53	F	T 6–T 10 unilateral
1933	Hartfall and Stewart[23]	Hereditary spherocytosis	52	F	T 7–T 10 bilateral
1935	Covey[10]	Erythroblastosis fetalis	17 days	M	T 5 left-sided
1936	Gleave[17]	Hereditary spherocytosis	28	M	T 3–T 9 bilateral
1945	Ask-Upmark[1]	Hereditary spherocytosis	70	F	T 8–T 11 bilateral
1958	Marinozzi[37]	Thalassemia intermedia	40	M	T 2–T 12 bilateral
1958	Foster[15]	Pneumonia	80	M	T 9–T 10 unilateral
1960	Coventry and LaBree[9]	Hereditary spherocytosis	50	M	T 8–T 11 bilateral
1960	Knoblich[29]	Thalassemia minor	63	M	T 5–T 11 bilateral
1960	Hanford *et al.*[21]	Hereditary spherocytosis	61	M	T 5–T 12 bilateral
		Hereditary spherocytosis	53	M	T 8–T 12 left-sided
1960	Litwer[32]	Hereditary spherocytosis	63	M	T 6–T 12 bilateral
		Hereditary spherocytosis	62	M	Low posterior mediastinum, bilateral
1962	Malamos *et al.*[36]	Thalassemia	24	M	T 2–T 10
1963	Lowman *et al.*[33]	Hereditary spherocytosis	43	M	Superior and inferior posterior mediastinum
		Hereditary spherocytosis	66	M	T 7–T 9
1964	Papavasiliou and Sfikakis[40]	Thalassemia	21	M	T 8–T 11 right-sided
		Thalassemia	28	M	T 10–T 11 right-sided
1964	Sorsdahl *et al.*[45]	Thalassemia intermedia	40	M	T 9–T 10 left side
		Thalassemia intermedia	45	M	T 8–T 9 left side
1964	Seidler and Becker[45]	Hemoglobin SS disease	31	M	T 8–T 11 mainly right-sided
1965	Drake *et al.*[13]	Hereditary spherocytosis	48	M	T 6–T 10 left sided

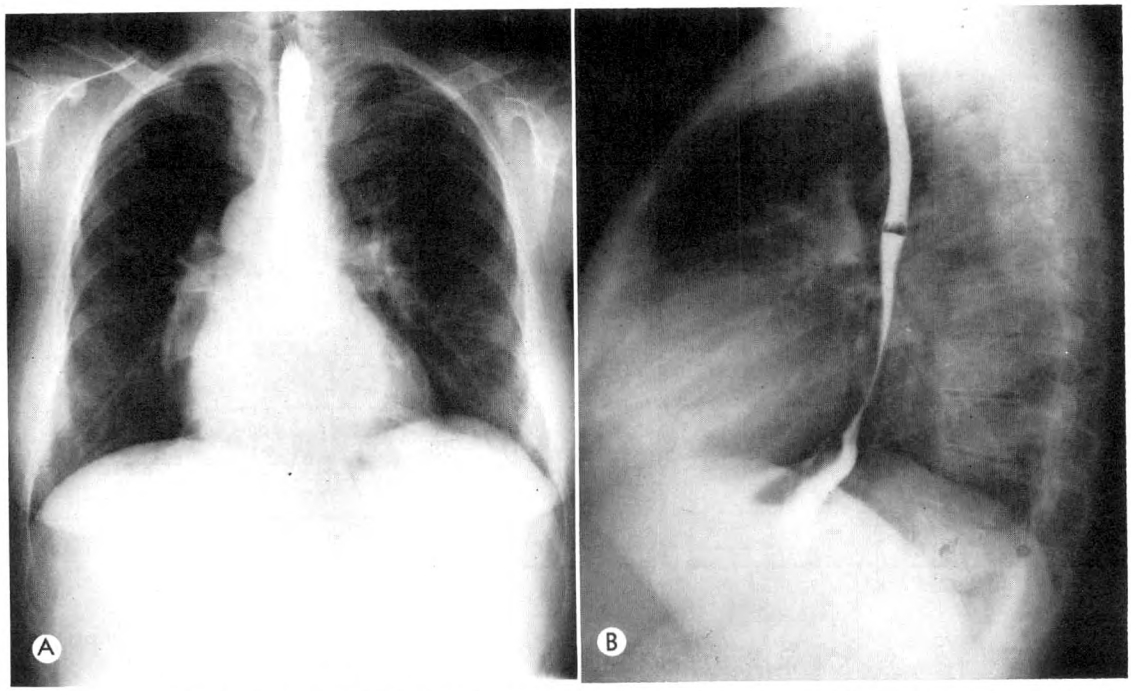


FIG. 1. Case 1. (*A*) Frontal and (*B*) lateral chest roentgenograms of a 24 year old female with thalassemia intermedia and lower extremity neurologic abnormalities. There is a large paraspinal bilateral lobulated soft tissue mass extending from T 2 to at least T 12. The size and appearance of the intrathoracic mass did not change following radiation therapy. Note the characteristic rib deformities of thalassemia.

and *B*) diagnosed as extramedullary hematopoiesis. A lateral skull roentgenogram (Fig. 2) revealed a "hair on end" widened diploic space, consistent with her severe chronic hemolytic anemia. On a nephrotomogram during an infusion intravenous pyelography (Fig. 3) bilateral peripelvic filling defects were noted. These were thought to represent extramedullary hematopoiesis. It was suggested that her neurologic symptoms were probably due to extramedullary hematopoiesis within the spinal canal. Lumbar mylograms demonstrated a complete block at the T 9–T 10 level (Fig. 4, *A* and *B*).

In view of the radiosensitivity of hematopoietic tissue and because surgical resection of such friable and vascular tissue is difficult, the involved area was treated with irradiation. A total tumor dose of 2,000 rads was delivered in 26 days. After an initial dose of 400 rads, 3 daily doses of 200 rads each were given to a 12 cm. by 22 cm. spinal area from T 3 to T 12. Twenty-four hours after the first treatment, the patient's gait had improved. On myelography at that time the block had been partially relieved. The radiation field was extended up to the C 3 level and down to the L 3 level, and 10 separate daily doses of 100 rads were delivered to the total enlarged area, followed by 5 daily doses of 200 rads to the C 3–T 3 and T 12–L 3 level areas only. She improved progressively and was able to wear high heels for the first time in a year. The free flow of pantopaque in the spinal canal was demonstrated at the end of radiation therapy, but there was persistence of a lobulated filling defect (Fig. 5, *A* and *B*). A splenectomy was performed. Abnormal tissue was palpated in the presacral region. A biopsy of this tissue was obtained and a metal clip was placed at the site for subsequent roentgenographic localization. On microscopic examination, it was reported that "this tissue is all hematopoietic—predominately erythropoietic. Megakaryocytes are fairly conspicuous, but none is noted to be as bizarre as the megakaryocytes usually seen in myeloproliferative disorders."

CASE II. C.A., a 26 year old Italian male was admitted to Strong Memorial Hospital at 1 year of age for evaluation of hepatosplenomegaly and failure to thrive. He was found to have thalassemia major. Since then he has re-

ceived 2 to 3 pints of packed red blood cell transfusions every 4 to 6 months. His growth was retarded but he has remained fairly compensated. Chest roentgenograms at 9 years of age were interpreted as normal. At 14 years of age repeat chest roentgenograms showed a lobulated lower thoracic bilateral paraspinal soft tissue mass which has since slowly enlarged (Fig. 6, *A* and *B*). This is thought to represent extramedullary hematopoiesis. No biopsy has been performed because the patient is asymptomatic, and since biopsying extramedullary hematopoietic tissue is dangerous.

Case III. A.A., a 13 year old Italian male who was evaluated at the age of 2 years for pallor and hepatosplenomegaly, was found to have thalassemia major. His hematocrit averaged 24 per cent and he had received 32 pints of blood by age of 4, at which time a splenectomy was performed. He has needed fewer transfusions since. A right paraspinal mass was noted on chest roentgenograms at the age of 12 (Fig. 7, *A* and *B*). He has no neurologic abnormalities and his condition is stable.

Case IV. S.R. was well until the age of 36 years when he was noted to be anemic. He was admitted to the Rochester General Hospital for evaluation and was found to have generalized lymphadenopathy and hepatosplenomegaly. His hematocrit was 37 per cent and the white blood cell count 13,200, with a shift to the left. The other laboratory tests were normal. A

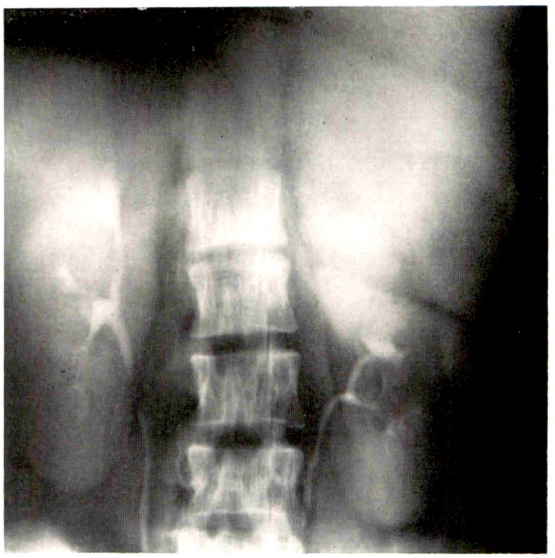


Fig. 3. Case 1. A nephrotomogram reveals peripelvic filling defects, more marked on the right, which were thought to be secondary to extramedullary hematopoiesis.

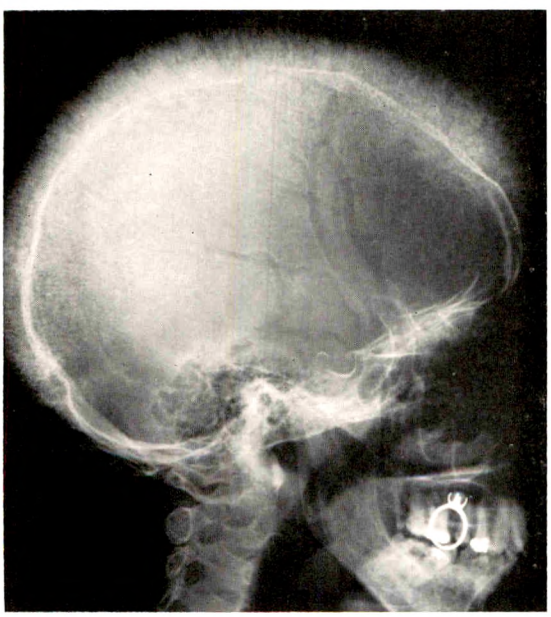


Fig. 2. Case 1. Lateral skull roentgenogram. The diploic space is very wide with "hair on end" appearance due to peripheral erythropoiesis.

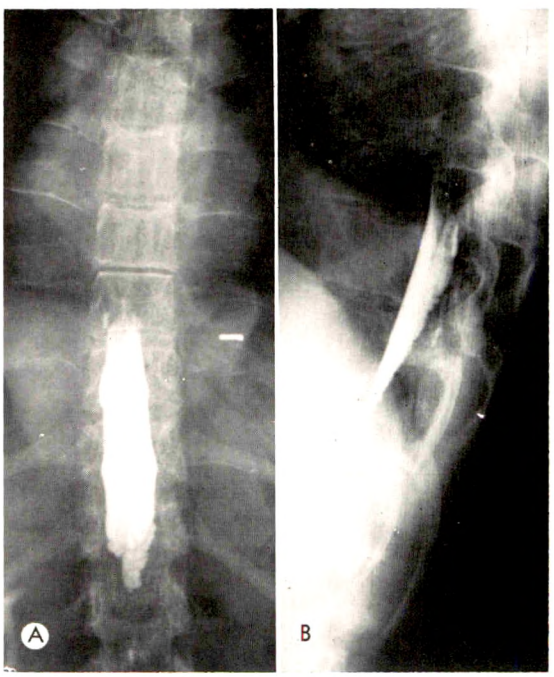


Fig. 4. Case 1. (*A* and *B*) Lumbar myelograms demonstrate a complete block to cephalad flow of pantopaque at the T 9–T 10 level.

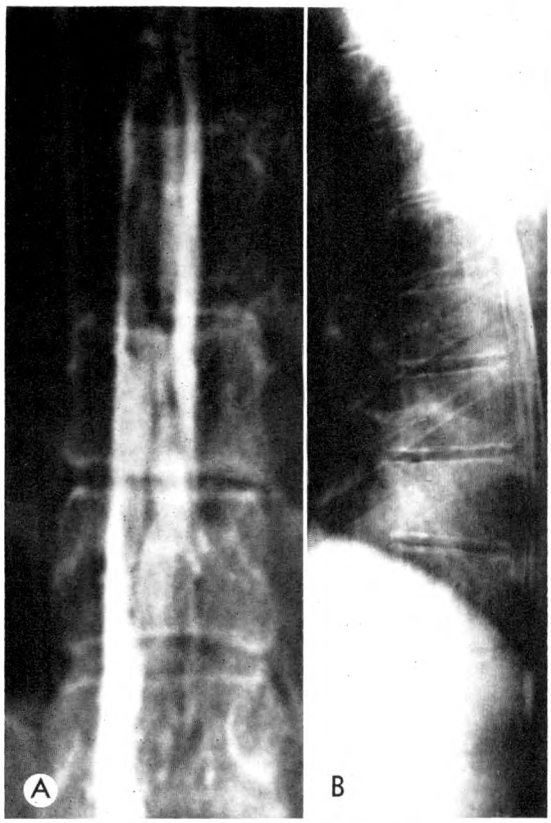


FIG. 5. Case 1. (*A* and *B*) Repeat myelograms at the end of radiation therapy demonstrate a persistent filling defect anteriorly, but free flow of pantopaque.

closed bone marrow biopsy was unsuccessful. An open iliac crest bone biopsy was then performed, revealing "only slight residual activity of the bone marrow, which is mostly sclerotic, with small foci of fibrosis." Groin and axillary lymph node biopsies were diagnosed as extramedullary hematopoiesis, with a microscopic evaluation revealing "lymph nodes largely replaced by intermingling fibrosis and fatty tissue. Within the former are scattered accumulations of neutrophils, lymphocytes and a few eosinophils. There are also occasional multinucleated giant cells with foamy cytoplasm within or outside of preserved lymphoid tissue. Many have lobulated nuclei and resemble megakaryocytes."

The consultant hematologist diagnosed the patient as having agnogenic myeloid metaplasia. A bone survey at this time demonstrated generalized patchy osteosclerosis and a chest roentgenogram revealed a large paraspinal intrathoracic mass, interpreted as extramedullary hematopoiesis (Fig. 8). An intravenous pyelogram (Fig. 9) showed distortion of the calyces, thought to be due to peripelvic extramedullary hematopoiesis. The patient became progressively anemic. At the time of his final admission 6 years later, his hematocrit was 17 per cent and he expired before transfusions could be performed. Unfortunately autopsy permission was refused.

PATHOGENESIS

The spleen and liver are favored sites for extramedullary hematopoiesis. They are not suitable, however, when they are hemolyzing abnormal erythrocytes.[21] Extramedullary hematopoiesis can then be expected to occur in other regions. The mechanism by which the thoracic hematopoietic masses are formed is uncertain. Embryonic rests have not been observed in this region. Replacement of lymph nodes by hematopoietic tissues seems improbable as there is no trace of lymph node structure on microscopic examination. It is unlikely that the pleura is responsible for the origin of the masses since it would be difficult to account for their constant location in the paravertebral region on this basis. Perhaps they are formed from branches of the intercostal veins,[1,8] or extrude from hypertrophied bone marrow, through the thinned trabeculae of the proximal ribs.[5]

ROENTGENOLOGIC FEATURES

In the thorax, the masses of extramedullary hematopoietic tissue are located in the posterior mediastinum often below the T 7 level. They may be unilateral or bilateral. The masses show well demarcated rounded margins, usually lobulated due to superimposition of several rounded densities. Occasionally the lateral contour forms a single curve. The medial margin merges with the mediastinum. No calcification or other variation in density is seen within the masses. Although they are very vascular they do not pulsate, and erosion or reactive change of the adjacent bone structures has not been described. However, there is a

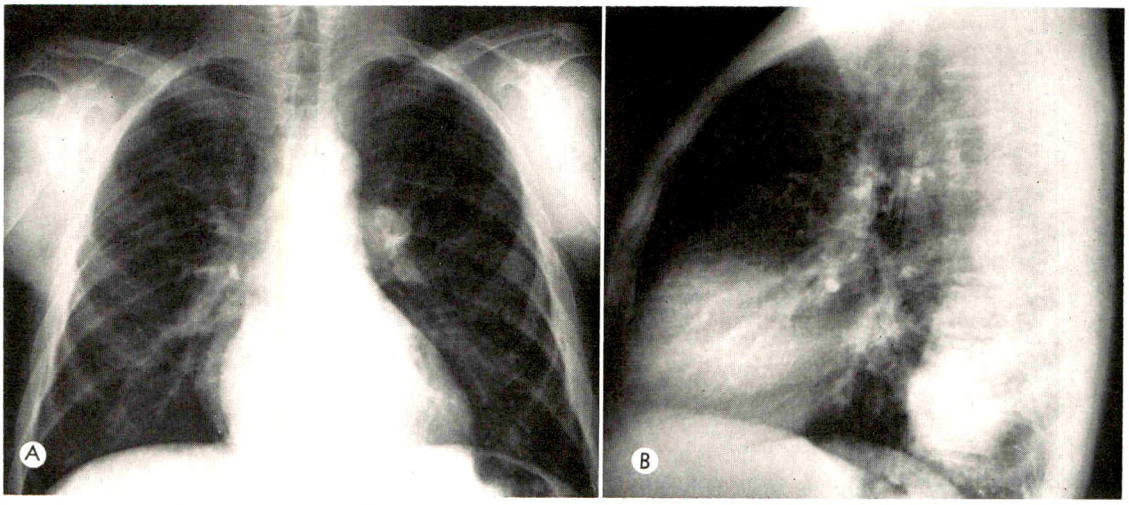


FIG. 6. Case II. (*A*) Frontal and (*B*) lateral chest roentgenograms of a 26 year old male with thalassemia major who has had a slowly growing bilateral lobulated paraspinal soft tissue mass extending from T 2 to T 11, first noted at age 14 and slowly enlarging since. The rib deformities are characteristic.

report of a bony mass containing hematopoietic tissue arising from the medial portion of the rib and eroding it.[5]

In the lateral view the main portion of the mass overlies the spine but the anterior margin is often visible as a sharply defined lobulated shadow. Posteriorly, the mass blends with the thoracic wall. Bucky roentgenograms using a spine technique, and tomograms may help to demonstrate the mass and to evaluate the adjacent bone structures.

Extramedullary hematopoietic masses do not show any marked decrease in size following splenectomy or radiation therapy.

DIFFERENTIAL DIAGNOSIS

1. *Neurogenic tumors.* Although these are the most common cause of a posterior mediastinal mass, at least 50 per cent show

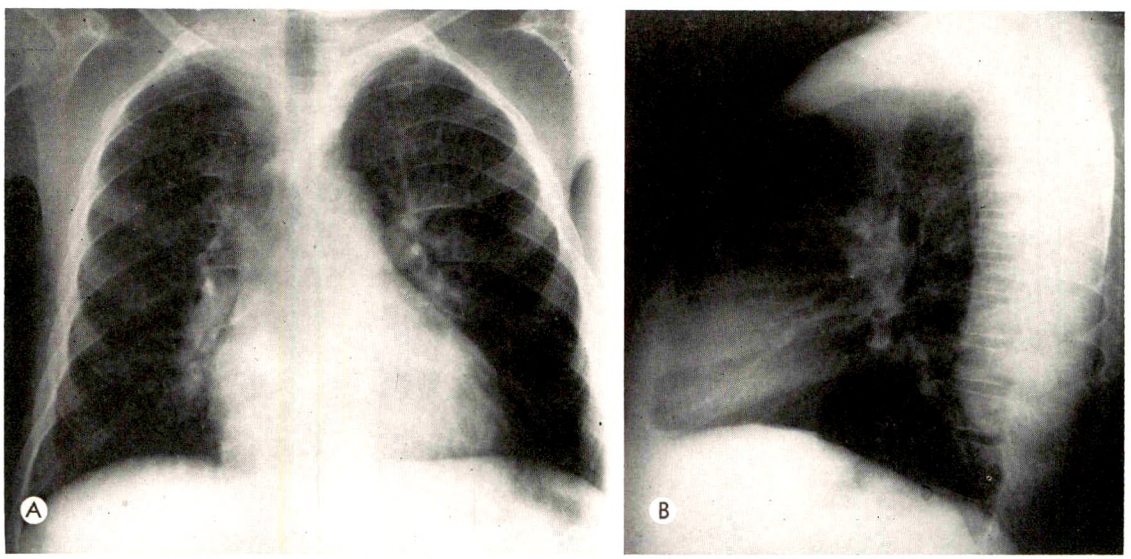


FIG. 7. Case III. (*A*) Frontal and (*B*) lateral chest roentgenograms of a 13 year old male with thalassemia major. Right paraspinal soft tissue mass extending from T 2 to T 11 is more evident in the lateral projection. Note the characteristic rib deformities.

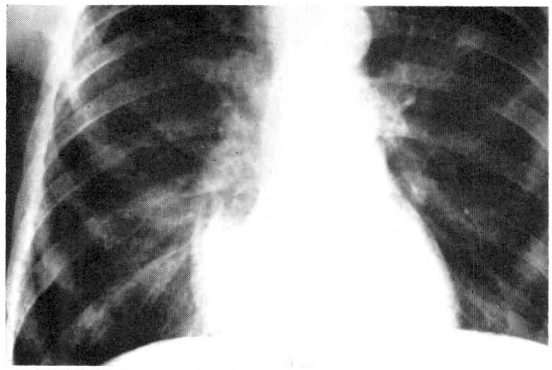


FIG. 8. Case IV. Frontal chest roentgenogram of a 36 year old male with myeloid metaplasia showing a large right paraspinal intrathoracic mass at the time of initial evaluation. This appearance did not change over the next 6 years, at which time the patient expired. Mixed osteosclerotic and osteolytic bone changes are present.

either erosion or sclerosis of the adjacent bone.[18] Usually the lateral margin of the tumor forms a smooth arc and it does not show any predilection for the lower thoracic region.

2. *Hodgkin's disease.* Although usually located in the middle or anterior mediastinum, lymphomatous masses are sometimes present predominantly in the paraspinal region of the thorax. The lateral margin is fusiform and occasionally lobulated. Contiguous osseous involvement was recognized on roentgenograms in 6 of 22 patients with a dorsal mediastinal mass of Hodgkin's tissue. Pain, often severe, was present in 19 of these 22 patients.[51] This is not a feature of extramedullary hematopoiesis. Hodgkin's tissue regresses markedly with adequate radiation therapy.

3. *Abscess arising from the spine.* Involvement of the bone structures can be demonstrated. No lobulation is present.

4. *Extrapleural cysts.* These produce a single arc at their anterior and lateral margins.

5. *Primary and metastatic malignancies.* These do not show a lobulated contour, and involvement of bone is common.

6. *Intrathoracic meningocele.* This presents as a single, or occasionally bilateral, round density. At least two-thirds of the cases are associated with neurofibromatosis and have vertebral deformities. Most of those not associated with neurofibromatosis also have vertebral defects.[31]

7. *Localized mediastinal lymph node hyperplasia.* Five cases of this entity have been described.[6,19,22,28,30] They present as a spherical or bosselated density, usually with a comparatively narrow attachment to the posterior mediastinum. Reactive change in the adjoining rib has been described.[48]

COMMENT

We have noted a peculiar, and, we believe, characteristic deformity in the ribs of our thalassemia patients. The vertebral ends of some of the ribs show a marked fusiform expansion over a length of about 3 cm. The inferior margin of the rib then curves upwards so that the rib has a normal height for 1 to 2 cm. and then its lower margin curves downwards again so that the remainder of the rib is fairly uniformly widened. In this way an appearance of a notch in the inferior margin of the ex-

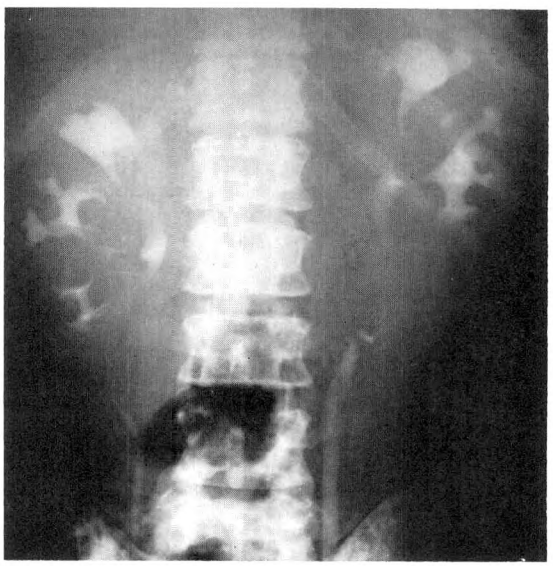


FIG. 9. Case IV. An intravenous pyelogram on the same patient as in Figure 8 reveals distortion of the collecting structures by peripelvic and periureteral filling defects. Again, the mixed osteosclerotic and osteolytic bone abnormalities are evident.

panded rib near its club-shaped vertebral end is produced (Fig. 1, *A* and *B*; 6, *A* and *B*; and 7, *A* and *B*). This configuration is evident in the published illustrations of the chest roentgenograms in several case reports dealing with thalassemia.[3,36,40] We have found it in 6 of the 14 thalassemia patients in whom chest roentgenograms were available for review. It was not present in the chest roentgenograms in any of our 21 patients with spherocytic hemolytic anemia or in 16 of our patients with sickle cell anemia.

DIAGNOSIS

The diagnosis of thoracic extramedullary hematopoiesis can confidently be made if the following four conditions are fulfilled.

1. A lobulated or rounded well demarcated soft tissue density is present in the paravertebral thoracic region, without erosion of the adjacent bone structures.
2. Roentgenographic bone changes of a condition which causes bone marrow abnormalities, such as chronic hemolytic anemia or myelofibrosis, are observed.
3. There is an enlarged spleen or a history of splenectomy.
4. A history of chronic anemia is obtained.

DISCUSSION

Case 1 is the second that we have been able to find in the literature in which a clinical diagnosis of spinal extramedullary hematopoiesis with compression of the spinal cord was suggested on the clinical grounds,[46] and the first in which this was confirmed by myelography and treated only by radiation therapy. The masses of hematopoietic tissue are notoriously vascular, and surgery should be avoided if at all possible. Even biopsy may be hazardous[21] and is unnecessary when the diagnostic critera are met. Two cases of extradural tumor masses of hematopoietic tissue over the brain have been reported,[25] and Brannan[2] described a case of a 7 month old infant with severe anemia whose falx cerebri was replaced by hematopoietic tissue. If a patient who has thoracic extramedullary hematopoiesis should develop signs of a cerebral tumor, the possibility of an intracranial hematopoietic mass must be considered. Arteriography may show a copious blood supply by way of the meningeal arteries.

The suggestion that the peripelvic infiltrate shown on intravenous pyelography in Cases 1 and 11 represents extramedullary hematopoietic tissue is attractive, since this has frequently been found at autopsy in patients with chronic anemia.[14,24,38,39,44,47] However, the appearance is not distinguishable from renal fibrolipomatosis. It is conceivable that Case 11 has developed a leukemic infiltrate of the kidneys, although there was no clinical evidence of leukemia at any time and he survived 6 years after the peripelvic densities were noted. Renal arteriography was not done since a definite diagnosis of renal extramedullary hematopoiesis has no practical importance.

CONCLUSIONS

From our experience with these cases and a review of the literature, we recommend:

1. Consider the possibility of extramedullary hematopoiesis in a patient who has chronic hemolytic anemia or myelofibrosis.
2. If the diagnostic tetrad described above is present, the mass should not be biopsied or removed because of the danger of hemorrhage.
3. If there are also neurologic symptoms, myelography is indicated.
4. If this shows a lesion which is not clearly due to another cause, the patient is assumed to have spinal extramedullary hematopoiesis and should be treated conservatively.

SUMMARY

1. A definite roentgenographic diagnosis of thoracic extramedullary hematopoiesis can be made if the patient has:

(a) a lobulated or rounded soft tissue density in the posterior mediastinum without rib erosion,

(b) roentgen changes in the bones of chronic hemolytic anemia or myelofibrosis,

(c) an enlarged spleen or a history of splenectomy, and

(d) a history of chronic anemia.

2. Extramedullary hematopoietic tissue may compress the spinal cord. Radiation therapy is effective.

3. A notched appearance of the expanded ribs seen only in patients with thalassemia is described.

4. Possibly peripelvic extramedullary hematopoietic tissue may mimic renal fibrolipomatosis.

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THE NEPHROGRAM: A VALUABLE INDICATOR OF RENAL ABNORMALITIES*

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THE use of excretory urography in the diagnosis of renal disease has advanced considerably since its introduction in 1929.[1] Improvements in contrast media have made it possible to obtain consistently high-quality roentgenograms with a very low incidence of serious side effects. The utilization of the nephrogram effect is not new, and has been previously emphasized in the diagnosis of renovascular hypertension,[5] obstructive uropathy,[4,10] and in the differentiation between cyst and neoplasm. Several attempts at obtaining early roentgenograms during excretory urography, to demonstrate the nephrogram phase, have been made.[6–9] However, such nephrograms were often faint because of poor timing, slow injection and/or inadequate volume of injected contrast material.

In most radiology departments, 5, 10 and 15 minute sequence films in an anteroposterior supine projection are exposed routinely. A further study in a prone position has been added in a number of departments to enhance the opacification of anteriorly located structures.[2]

The purpose of this paper is to recommend as part of routine excretory urography, a 20 second roentgenogram in order to obtain a maximum-intensity nephrogram, to describe the technique used in securing such a study, and to illustrate some of the applications of the nephrogram in diagnostic uroradiology.

TECHNIQUE OF EXAMINATION

1. A preliminary 14×17 inch roentgenogram is exposed in the anteroposterior projection.
2. Fifty milliliters of 50 per cent sodium diatrizoate is injected into one of the antecubital veins as rapidly as possible, using an 18 gauge needle. The injection time should be no more than 20 seconds.
3. Twenty seconds after the end of the injection, a roentgenogram of the kidneys is exposed in an anteroposterior projection on an 11×14 inch film.
4. Studies are obtained at 5, 10 and 15 minutes to complete the examination.

Ureteral compression is not necessary. A cleansing enema or a cathartic given the evening before the examination is advisable. A light breakfast is allowed, with restriction of fluids preferable. The volume of contrast medium given is not as critical as the length of time of injection. The rapid injection of contrast material has not increased our incidence of untoward reactions.

With the above technique, an excellent nephrogram on the 20 second roentgenogram, far better than that seen in any 5, 10 or 15 minute study, will be obtained consistently.

REPORT OF CASES

DOUBLE COLLECTING SYSTEM

CASE I. D. T., a 42 year old Negro female, had an excretory urogram to evaluate a possible renovascular cause for her hypertension. The 20 second nephrogram (Fig. 1*A*) showed a smooth renal outline with 2 indentations on the medial border of the kidney, indicating the presence of a double collecting system.

CASE II. A. D., a 49 year old female, was admitted to the hospital because of a pelvic mass. An excretory urogram was obtained to demonstrate the effect of the mass on the urinary

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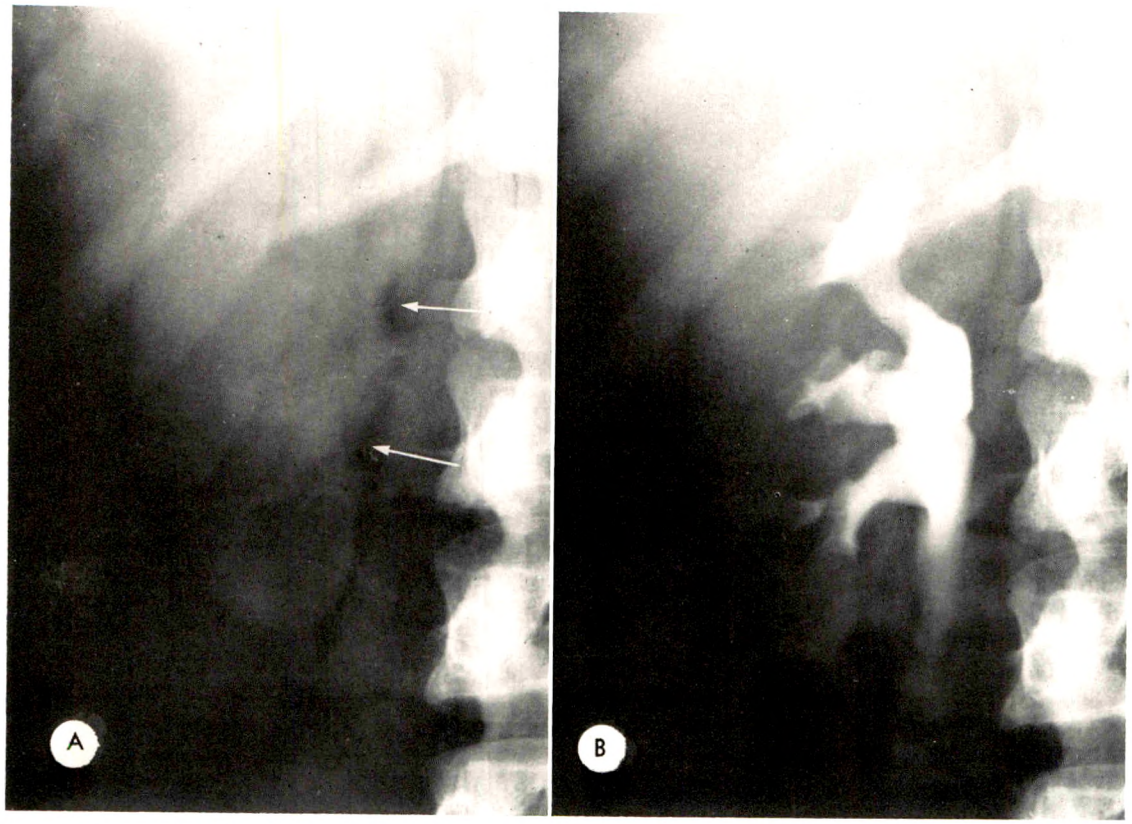


Fig. 1. Case 1. (*A*) Twenty second nephrogram shows smooth renal outline with 2 indentations (arrows) on the medial border of the kidney indicating the presence of a double collecting system. (*B*) A 5 minute study confirms the presence of a double collecting system (bifid renal pelvis). There is slight pelvicalyceal dilatation.

tract. The 20 second nephrogram (Fig. 2*A*) showed 2 areas of radiolucency representing areas of peripelvic fat, and a straight medial border of the kidney, without any indentation.

Comment. The normal renal outline is usually smooth, with the exception of the medial border where a single indentation or recess is seen representing the renal hilum. About the renal pelvis is the peripelvic fat, a normal constituent of the renal hilum.

The roentgen criteria for a double collecting system on the nephrogram are as follows: (a) a straight medial border of the kidney; or (b) 2 indentations on the medial border of the kidney (Fig. 1, *A* and *B*); and/or (c) 2 areas of radiolucency due to 2 distinct areas of peripelvic fat (Fig. 2, *A* and *B*).

The other conditions which may cause a straight medial border of the kidney are certain malrotations and a completely extrarenal pelvis.

"Pancake" kidney

Case III. F. B., a 57 year old female who complained of urinary dribbling was evaluated in another hospital, where a diagnosis of "horseshoe kidney" was made. An excretory urogram with a 20 second nephrogram (Fig. 3*A*) showed a solitary ovoid mass in the pelvis. Cystoscopy and retrograde urography (Fig. 3*B*) revealed only 1 ureteral orifice.

Comment. The nephrogram was of great aid in establishing the exact type and location of the renal anomaly. The subsequent roentgenograms (5, 10 and 15 minutes) showed only the collecting system, which is similar to that seen in a pelvic "horseshoe" kidney.

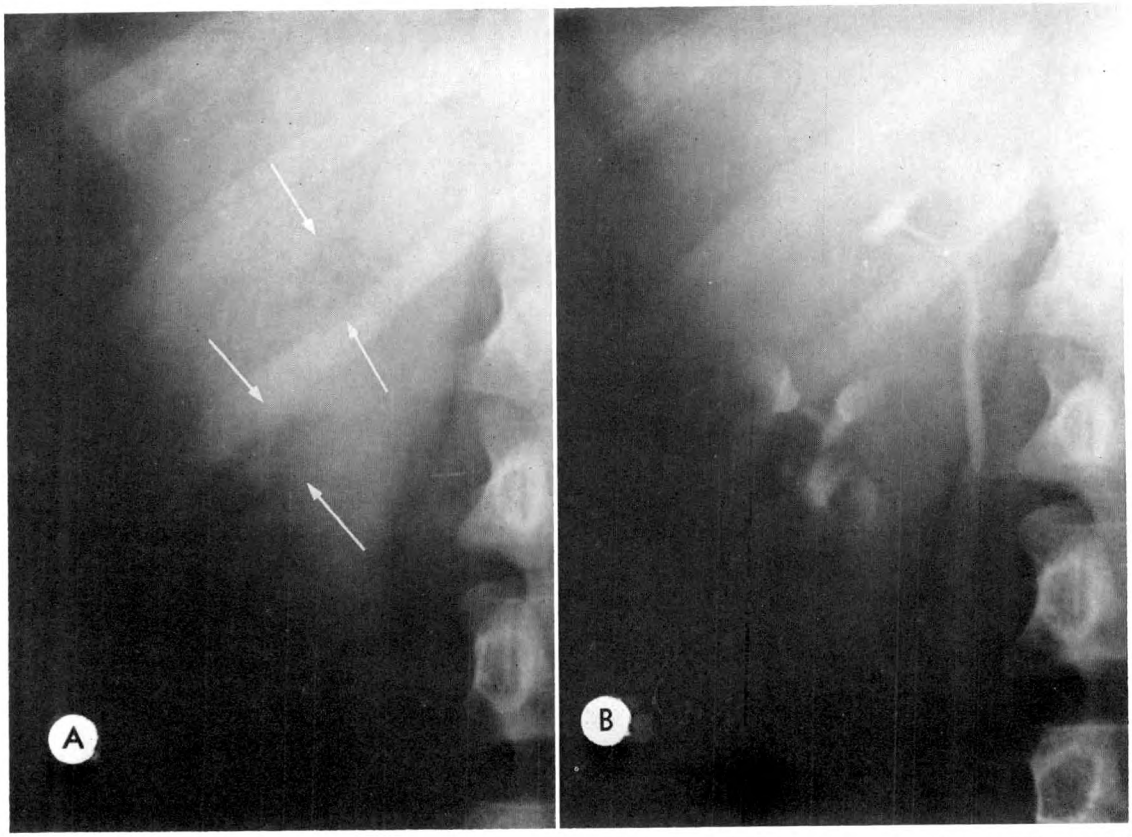


FIG. 2. Case II. (*A*) Twenty second nephrogram shows 2 areas of radiolucency (arrows) and a straight medial border of the kidney. (*B*) A 5 minute study shows a double collecting system. It is apparent that the radiolucencies seen in *A* represent 2 areas of peripelvic fat.

A "pancake" kidney represents a rare congenital anomaly of renal size, shape and position. All reported cases have been in a pelvic location. It may be associated with 1 or 2 ureters. In the latter instance, there is complete renal fusion.

TRAUMA

CASE IV. A. M., a 27 year old male, was admitted with a rigid abdomen and gross hematuria following a gunshot wound. An excretory urogram (Fig. 4, *A* and *B*) was performed, and the 20 second nephrogram showed obliteration of the upper lateral border of the left kidney with collections of opaque medium in the midportion of the kidney, indicating interstitial extravasation.

Exploratory laparotomy revealed a shearing of the cortex on the upper lateral aspect of the left kidney, a splenic laceration, perforation of the gastrocolic omentum and a hematoma of the mesentery.

Comment. The nephrogram in cases of trauma is, on occasion, the only study that will show the presence and extent of a renal injury. This is well demonstrated in cases of "hairline" fracture of the kidney, where the nephrogram will show the kidney to be normal or slightly enlarged, with a peripheral radiolucent line due to blood dissecting the cortex. The collecting system in such cases usually appears normal.

CHRONIC PYELONEPHRITIS

CASE V. M. P., a 76 year old female, was admitted to the hospital with a 3 day history of fever, chills, left costovertebral angle tenderness, dysuria, burning and frequency. There was a documented history of previous urinary tract infection. Excretory urography was performed, and the 20 second roentgenogram (Fig. 5) showed lobulation of the renal outline with a "spotty" irregular nephrogram, indicating chronic pyelonephritis.

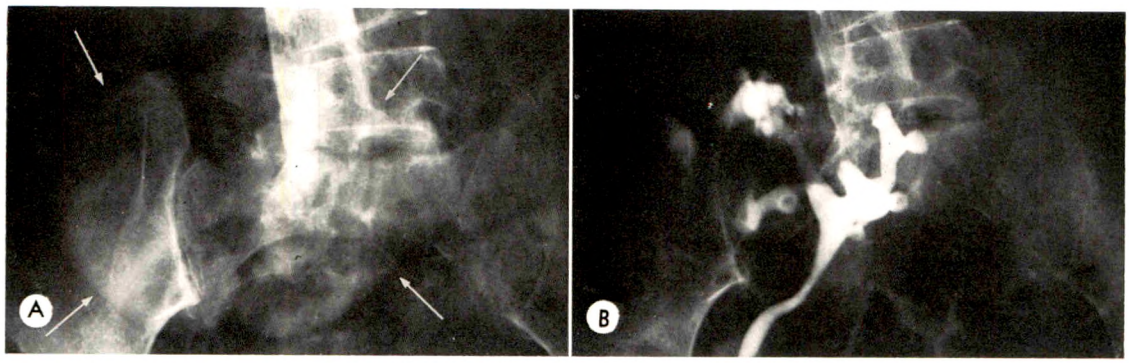


Fig. 3. Case III. "Pancake kidney." (*A*) A 20 second nephrogram shows an ovoid renal mass overlying the sacrum (arrows). (*B*) Retrograde pyelogram shows the antler-like configuration of the collecting system. Only one ureteral orifice was seen on cystoscopy.

Comment. The roentgen diagnosis of chronic pyelonephritis can at times be difficult. The 20 second nephrogram (Fig. 5) will contribute to the diagnosis by demonstrating an uneven, "spotty" nephrogram (due to alternating areas of normal and diseased parenchyma) and a lobulated renal contour due to scarring.

NEOPLASM AND CYST

Case VI. A 62 year old male was hospitalized because of prostatic enlargement. Excretory

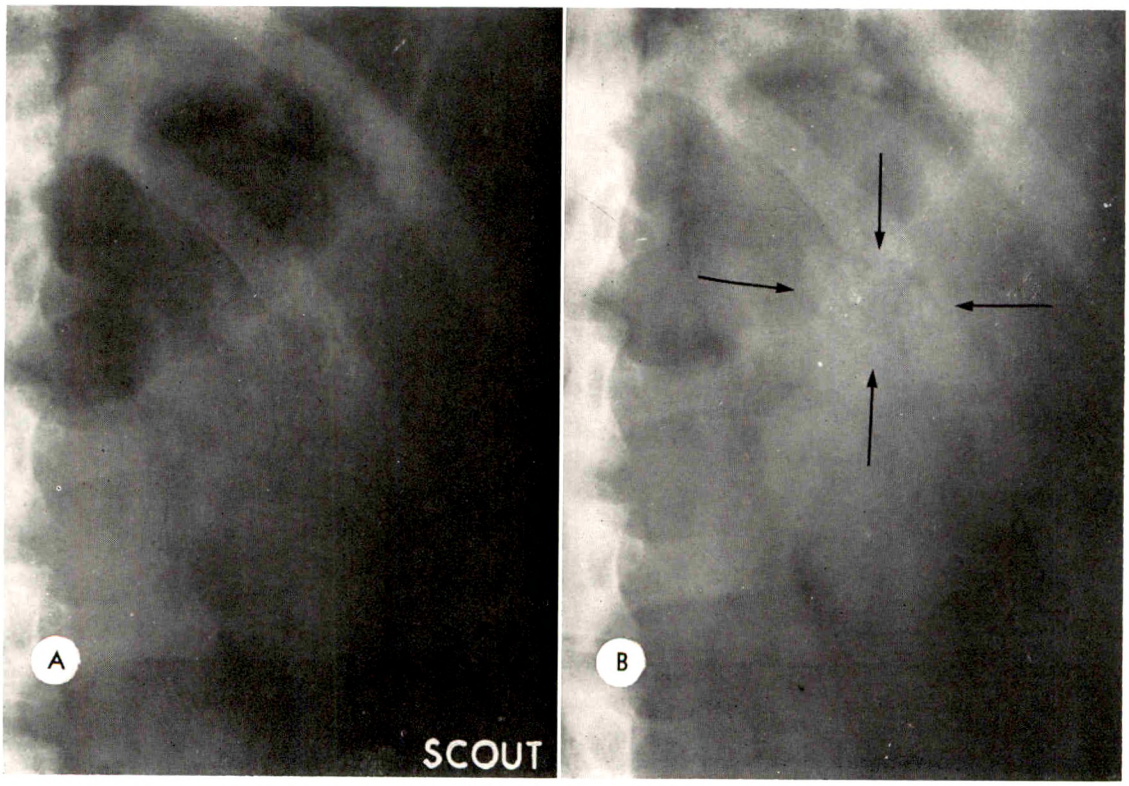


Fig. 4. Case IV. Trauma. (*A*) A preliminary plain roentgenogram shows a fracture of the left twelfth rib. (*B*) A 20 second nephrogram shows obliteration of the upper lateral border of the left kidney. Numerous small, patchy densities (arrows) are present in the midportion of the kidney overlying the fracture site, indicating interstitial extravasation of contrast medium.

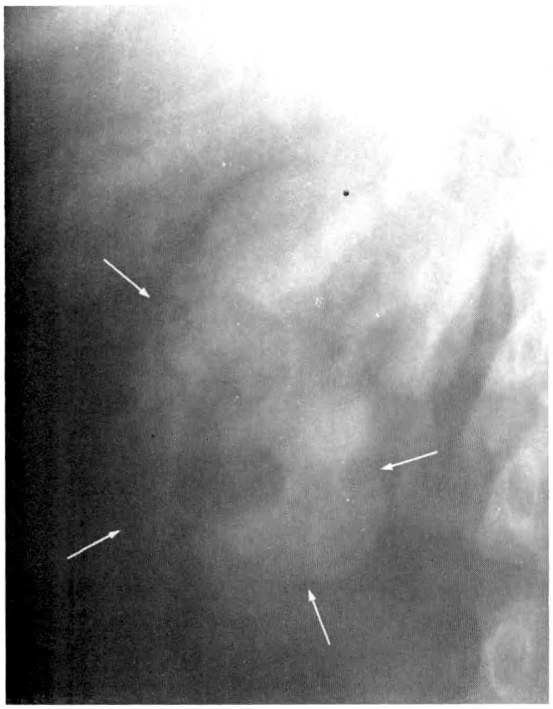


FIG. 5. Case v. Chronic pyelonephritis. Twenty second study shows lobulation of the renal outline (arrows) and a spotty, irregular nephrogram.

urography (Fig. 6, *A* and *B*) showed a slight hump in the suprahilar region of the right kidney associated with deformity of the upper calyx. The 20 second nephrogram (Fig. 6*A*) showed the lesion to be of equal or greater density than the normal renal parenchyma, thus suggesting the presence of a neoplasm, which was corroborated by renal angiography (Fig. 6, *C* and *D*).

Comment. The 20 second nephrogram can be utilized in the differential diagnosis of cyst and neoplasm using the same criteria applied in nephrotomography. A cyst will appear as a homogeneously smooth, well circumscribed, radiolucent lesion in the nephrogram. A neoplasm will present as a poorly outlined mass, with irregular areas of density, due to new vessel formation in the tumor. Without the use of the nephrogram, both cyst and neoplasm will present in the excretory urogram with the same density and their differentiation will be difficult, if not impossible.

This case demonstrates the importance of proper timing (at 20 seconds) of the nephrogram. In a few minutes, a hypervascular neoplastic lesion may become radiolucent against the background of a normal tubular nephrogram, due to rapid arteriovenous shunting of contrast medium in the malignant tumor (Fig. 6*B*).

HYDRONEPHROSIS

CASE VII. E. B., a $4\frac{1}{2}$ year old girl, was hospitalized because of a mass of the right side of the abdomen of approximately 5 months' duration. On excretory urography (Fig. 7, *A* and *B*) the nephrogram phase showed an enlarged renal outline with multiple well circumscribed radiolucencies, which became opaque on a delayed study. These findings indicate the presence of hydronephrosis.

Comment. The nephrogram thus contributes an important roentgen sign of hydronephrosis which consists of multiple well circumscribed radiolucencies (due to the dilated, urine-filled calyces) eventually opacifying on delayed roentgenograms.

SEGMENTAL INFARCT

CASE VIII. G. G., a 65 year old female with known rheumatic heart disease and atrial fibrillation, was hospitalized because of sudden persistent severe left flank pain.

Urinalysis showed 2+ albumin and 3–4 red blood cells per high power field. An emergency excretory urogram with a 20 second roentgenogram (Fig. 8*A*) showed an area devoid of a nephrogram at the lower pole of the kidney with an irregular border. The 5 minute roentgenogram showed a normal collecting system (Fig. 8*B*). A selective left renal arteriogram (Fig. 8*C*) demonstrated an embolus to the ventral branch of the renal artery in the arterial phase and a nephrogram (Fig. 8*D*) similar to that seen on the 20 second study of the excretory urogram.

Comment. The diagnosis of segmental renal infarct on routine excretory urography is difficult. However, with the 20 second nephrogram, segmental infarcts can be shown clearly by demonstrating a homogeneous nephrogram of the uninvolved portion of the kidney, with a grossly ir-

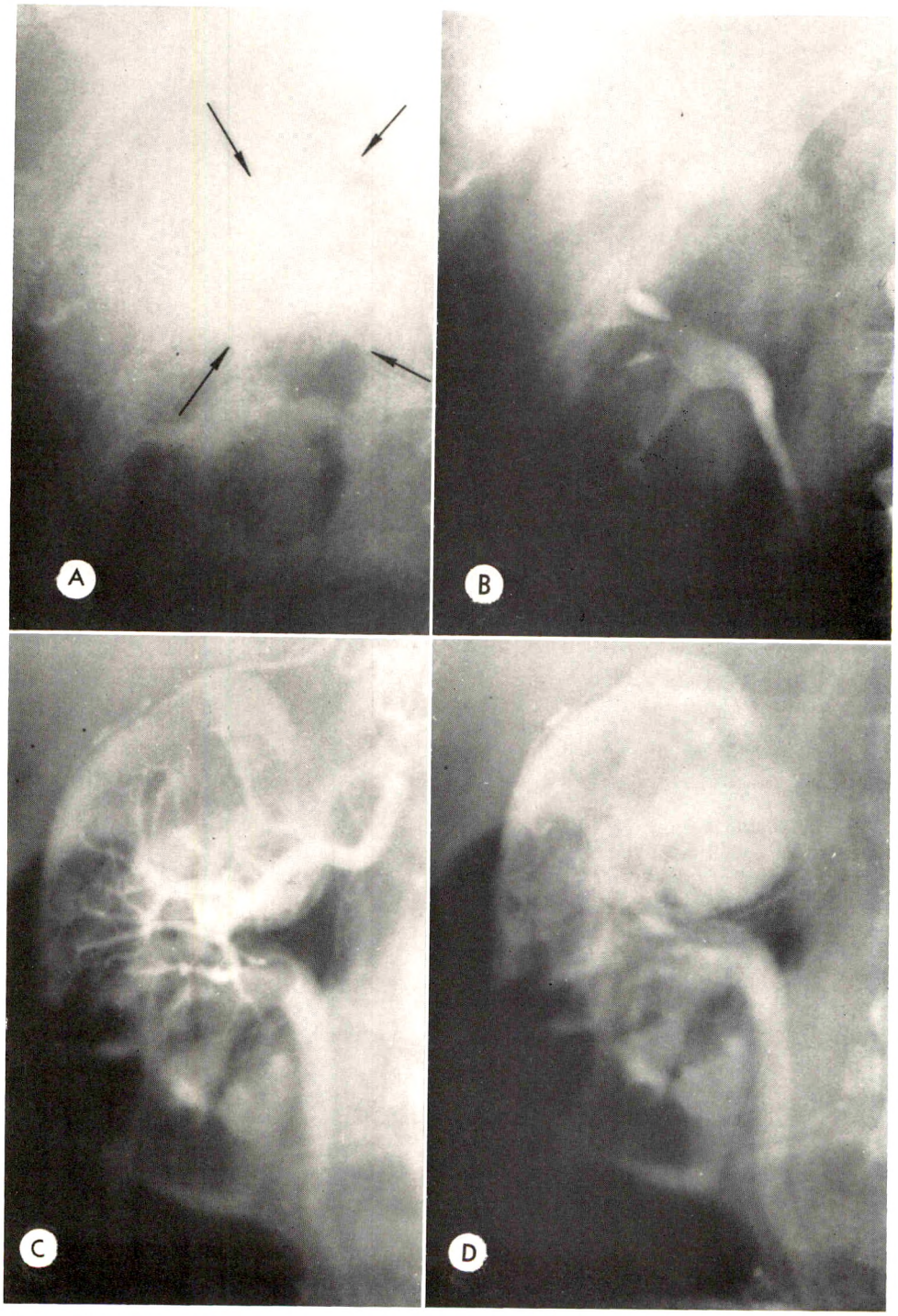


Fig. 6. Case vi. Neoplasm. (*A*) A 20 second nephrogram shows a slight bulge of the right suprahilar region, due to a spheroid mass of increased density (arrows). (*B*) A 5 minute roentgenogram shows deformity of the upper pole calyx adjacent to the tumor. At this time the lesion appears relatively radiolucent against the background of the normal tubular nephrogram, due to rapid arteriovenous shunting of contrast medium. (*C* and *D*) Selective renal arteriograms show neovasculature in the lesion indicating the presence of a carcinoma, verified at operation.

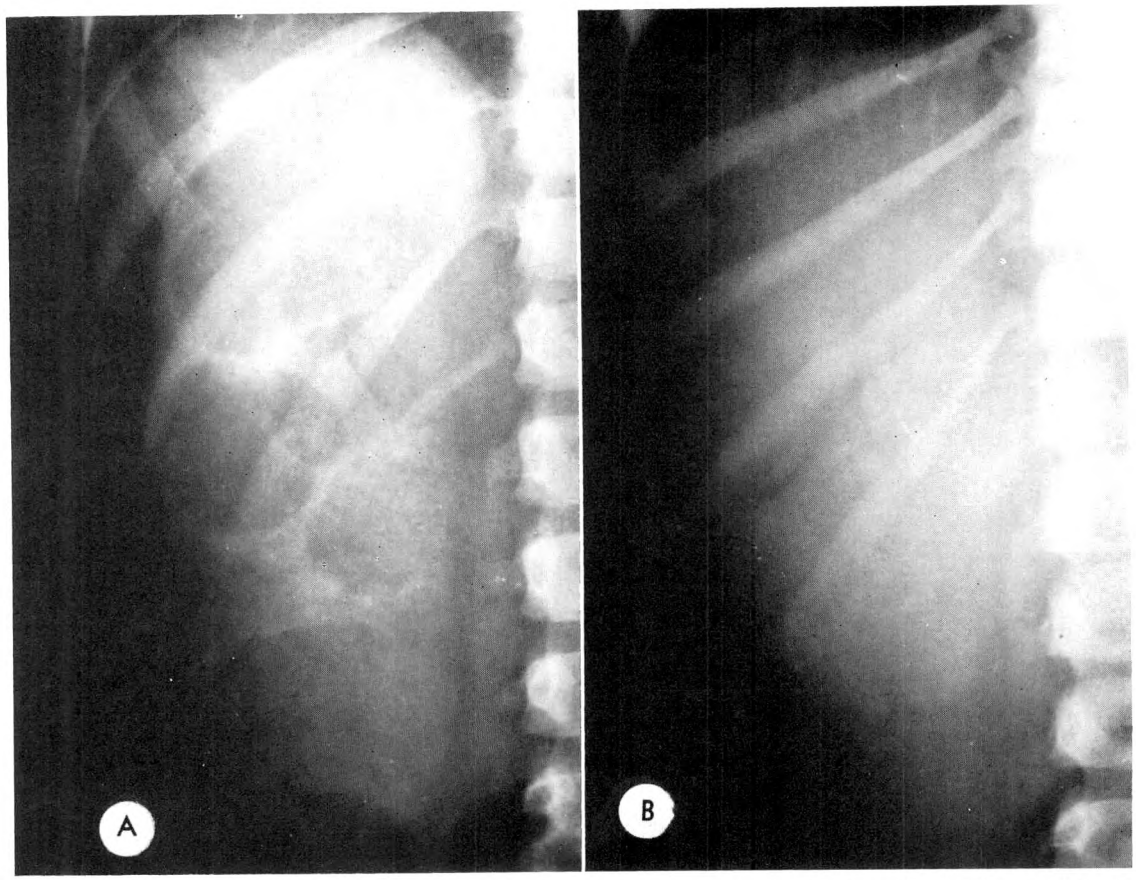


FIG. 7. Case VII. Hydronephrosis. (*A*) The nephrogram shows an enlarged renal outline with some lobulation. Multiple well-circumscribed radiolucencies are present. (*B*) A 24 hour study shows opacification of the previously radiolucent areas due to accumulation of contrast material in the markedly dilated calyces.

regular border demarcating the area of the infarct, which is devoid of a nephrogram.

DISCUSSION

The term nephrogram refers to the opacification of renal parenchyma during any roentgen examination. There are several types of nephrograms. The nephrogram seen during routine excretory urography is due mostly to the presence of contrast medium in the various elements of the nephrons as it is being excreted. This type of nephrogram is called the *tubular nephrogram*, produced mainly by glomerular filtration. A very small portion of the nephrogram seen in intravenous urography may be due to the opacified blood in the kidney—the *vascular nephrogram*. Although prominent in renal angiography, the vascular nephrogram plays a minor role in excretory urography, where it is a fleeting phenomenon, appearing with a normal circulation time about 12 seconds after the injection and disappearing after a few seconds.

In cases of obstruction, a different mechanism is responsible for the production of the nephrogram. The obstructed kidney will show progressive opacification due to the accumulation of contrast medium in the tubules and tubular cells and, to some extent, in the interstitial tissues of the kidney, resulting in the *obstructive nephrogram*. This effect is produced mainly by tubular secretion, although some glomerular filtration occurs.

During circulatory collapse, glomerular filtration is hindered by a fall in glomerular

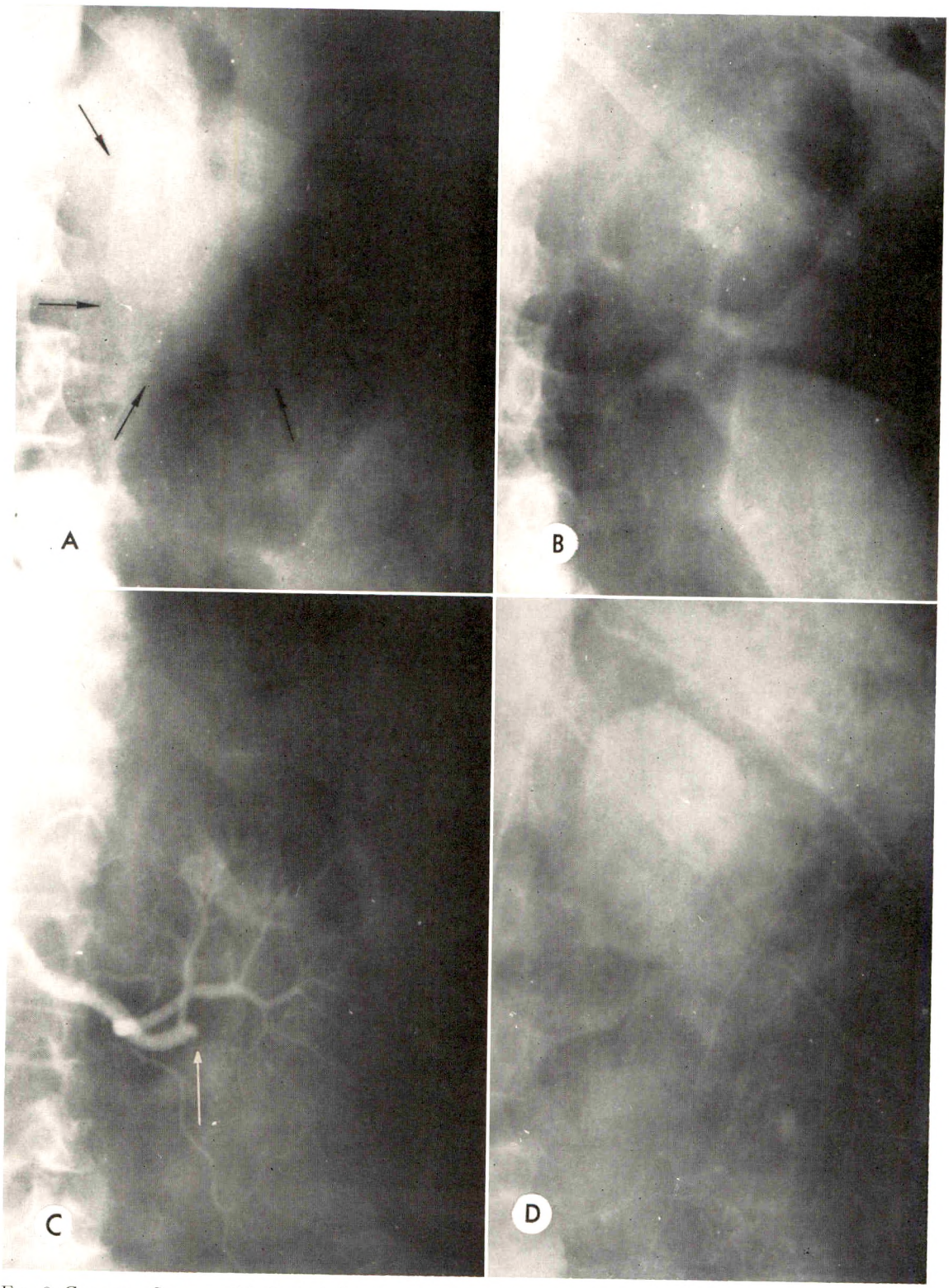


FIG. 8. Case VIII. Segmental infarct. (*A*) A 20 second roentgenogram shows absence of a nephrogram in the lower pole and a normal nephrogram (arrows) in the upper pole. An irregular border separates the 2 areas. (*B*) A 5 minute study shows a normal collecting system. (*C*) A selective left renal arteriogram shows an embolus to the ventral branch of the main renal artery (arrows). (*D*) A delayed arteriogram shows a lack of a nephrogram effect in the lower pole, similar to that seen in the 20 second study.

capillary pressure. Under these circumstances, tubular secretion continues, and contrast medium accumulates in the same sites as in the obstructive nephrogram. The nephrogram seen in these cases is called the *hypotensive nephrogram*.[3]

With our increasing knowledge of the effects of contrast media on renal physiology, a more selective program for excretory urography is possible. Also, renal abnormalities previously undiagnosable during routine excretory urography can now be demonstrated with the use of more select studies. The 20 second roentgenogram will show an excellent nephrogram that provides important information regarding size, contour and defects of the kidney. Congenital anomalies (fused, solitary, or ectopic kidneys, malrotations and duplications) and many acquired renal diseases may thus be studied to better advantage.

The 15 minute roentgenogram can be omitted from routine excretory urography since the 5, 10 and 15 minute roentgenograms show essentially the same segments of the upper urinary tract. The examination can be terminated ordinarily at 10 minutes if it is normal, thereby saving valuable time, or variations in timing after the 10 minute study can be instituted, depending on the findings in the individual case.

SUMMARY

A simple technique to obtain an excellent nephrogram is presented. The additional valuable information that can be obtained from a 20 second nephrogram is discussed and illustrated and the inclusion of the 20 second roentgenogram in routine excretory urography is recommended.

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INTRAVENOUS UROGRAPHY IN RENAL INSUFFICIENCY*

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THE traditional concept that excretory urographic studies of diagnostic quality can be obtained only in patients with normal or near normal renal function has been challenged repeatedly in recent years. Doyle and associates,[6] Ross and coworkers,[11] Bloomfield,[4] Friedenberg and Carlin,[8] and others have demonstrated that by using large doses of modern contrast medium, excretory urograms of diagnostic quality can be obtained without increased hazard in many patients with depressed renal function who in the past were not considered candidates for this examination.

The experience of these authors has prompted us to study a broad spectrum of patients with depressed renal function of varied severity and etiology in an effort to clarify the relationships between the degree of renal function impairment and the ability to demonstrate renal anatomy, and to gather data on the effect of large doses of excretory urographic medium on renal function. Continuing advances in the medical and surgical treatment of renal and urologic diseases have created a need for urographic techniques capable of safely providing useful information in patients with impaired renal function.

MATERIAL AND METHOD

Fifty-five patients (39 males and 16 females) with impaired renal function whose ages ranged from 5 to 83 years were studied. All patients had excretory urographic studies and determination of either serum creatinine or endogenous creatinine clearance (or both) as an index of their renal function. The serum creatinine concentration and the endogenous creatinine clearance are considered by many as the most reliable and yet practical routine indicator of renal function.[5,7,16]

Patients were considered to have impaired renal function if the level of serum creatinine was greater than 1.15 mg./100 ml. or the endogenous creatinine clearance was less than 50 ml./min./1.73 sq. m. corrected for body surface. The accepted range of normal serum creatinine at the Mayo Clinic for females is 0.6 through 0.9 mg./100 ml., and for males 0.8 through 1.2 mg./100 ml.

The value for blood urea was not used as a criterion of impaired renal function because it has been demonstrated that various factors unrelated to renal function can produce wide variations in the levels of blood urea and that the correlation between this determination and renal function as measured by other techniques is poor.[1,16]

In this series 55 patients underwent 66 urographic examinations. Serum creatinine values of these patients ranged from 1.15 mg. through 19.5 mg./100 ml. For analysis, the 55 patients were arbitrarily divided into 4 general groups on the basis of the serum creatinine value: Group 1, serum creatinine of 1.15 through 2.9 mg./100 ml. (21 examinations); Group 2, serum creatinine of 3.0 through 4.9 mg./100 ml. (22 examinations); Group 3, serum creatinine of 5.0 through 6.9 mg./100 ml. (12 examinations); and Group 4, serum creatinine greater than 7.0 mg./100 ml. (11 examinations).

Twenty of the 55 patients had determinations of either serum creatinine or

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creatinine clearance (or both) before and after the urographic examination. The pre-urographic study values were obtained from 1 to 3 days prior to the examination, and the posturographic study values were obtained within 2 weeks. All but two of the determinations made after the urographic examination were done within 6 days.

This study is composed of patients with a wide range of diseases commonly associated with depressed renal function. The clinical diagnoses made in the 55 cases included chronic pyelonephritis (14 patients), renal insufficiency of undetermined cause (14 patients), chronic glomerulonephritis (10 patients), extrarenal obstructive uropathy (6 patients), diabetes mellitus (3 patients), primary hyperparathyroidism (2 patients), Wilson's disease (1 patient), renovascular disease (1 patient), polycystic disease (2 patients), multiple myeloma (1 patient), and congenital absence of abdominal muscles (1 patient).

All patients were studied by means of at least 1 of 3 urographic techniques. Twenty-four examinations were done in 22 patients who were not known to the radiologist to have had impaired renal function prior to the urographic examination. In these patients, the initial urographic study consisted of conventional intravenous urography using 30 ml. of a 69 per cent solution of meglumine and sodium diatrizoate (renovist) as the contrast agent. Conventional plain film roentgenography was supplemented by tomography in patients who had satisfactory demonstration of the urinary-collecting system but inadequate demonstration of the renal parenchyma with this dose of contrast medium.

In 14 examinations, the conventional dose of urographic medium failed to opacify the urinary tract with enough clarity for diagnosis. Twelve of these patients were immediately re-examined using a dose of 50 ml. of a 90 per cent solution of meglumine and sodium diatrizoate (hypaque-M) supplemented by tomography. In the other 2 patients, no further examinations were carried out.

Forty-two examinations were performed in 39 patients with known renal function impairment of varied degrees. This group was studied with a drip-infusion technique that used 100 ml. of 90 per cent solution of meglumine and sodium diatrizoate (hypaque-M) either with or without dilution in an equal volume of 5 per cent dextrose in water. Tomograms made at levels encompassing the full thickness of the kidney, to further enhance the demonstration of anatomic detail, were obtained routinely when the increased doses of contrast media were used.

The anatomic visualization obtained in each of the 66 roentgenographic examinations was reviewed and correlated with (1) the type of examination performed and (2) the various degrees of renal insufficiency, as indicated by the serum creatinine value.

The quality of visualization of the renal parenchyma, calyces, and ureters was assessed and categorized as good, satisfactory, poor, or no visualization (Table 1).

In tabulation of the results (Fig. 1), an examination in which visualization was good or satisfactory is listed as of diagnostic quality. One in which visualization was poor or in which there was no visualization was listed as nondiagnostic. However, even in those examinations in which opacification was poor and in those in which no visualization of a portion of the urinary tract was obtained, useful information on the status of the kidneys was provided.

RESULTS

Although in many of the examinations the roentgenographic density of the contrast medium in the renal parenchyma and collecting system was not great, and in other examinations a portion of the urinary tract was not opacified (through the use of one or more of the techniques previously described), significant information could be obtained concerning the gross anatomy and pathology of the kidneys in all 66 urographic examinations.

Table I

CRITERIA FOR ROENTGENOGRAPHIC EVALUATION

Renal Parenchyma

Good—entire outline of the kidney well seen
Satisfactory—renal parenchyma seen with enough clarity to detect cortical thinning and to rule out a mass lesion
Poor—insufficient detail to exclude a parenchymal mass lesion
No visualization

Calyces

Good—all calyces filled and the fine details of anatomy demonstrated
Satisfactory—calyces seen with enough clarity to recognize blunting and calyceal displacement
Poor—calyces incompletely filled
No visualization

Ureters

Good—both ureters seen in their entirety on the series of roentgenograms
Satisfactory—renal pelvis and upper one-third of ureters demonstrated well enough to rule out ureterectasis
Poor—ureter seen but not well enough to rule out ureterectasis
No visualization

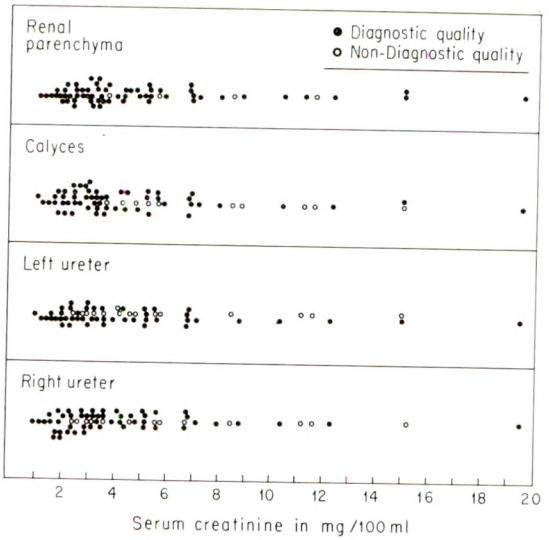


Fig. 1. Relationship between anatomic visualization and serum creatinine values.

Table II shows a comparison between the type of roentgen examination performed and the diagnostic quality of the examination.

CONVENTIONAL UROGRAPHY WITH OR WITHOUT TOMOGRAPHY

Among the 24 conventional excretory urographies that were the initial examination done in 22 of our patients (2 were examined on 2 separate occasions), demonstration of renal anatomy was adequate for roentgenographic diagnosis without further study in 5. Tomography was needed to supplement the plain film roentgenographic examination in 5 additional cases when the calyces but not the renal parenchyma were clearly seen on plain film roentgenograms. In 2 additional patients, the study was terminated with conventional urography, even though demonstration of renal anatomy was not complete. The serum creatinine values ranged from 1.75 through 11.3 mg./100 ml., and in 11 patients in whom the creatinine clearance was determined, it ranged from 4.8 through 46 ml./min./1.73 sq. m. In the 2 examina-

Table II

COMPARISON OF TYPE OF ROENTGEN EXAMINATION WITH DIAGNOSTIC QUALITY OF UROGRAM

Type	No. of Urograms	Renal Parenchyma Visualized		Calyces Visualized		Ureter(s) Visualized	
		Yes	No	Yes	No	Yes	No
Conventional urogram	24						
Without tomogram		5	2	5	2	6	1
With tomogram		5	0	4	1	4	1
Plus reinjection		12	0	10	2	12	0
Infusion	42	40	2	37	5	36	6

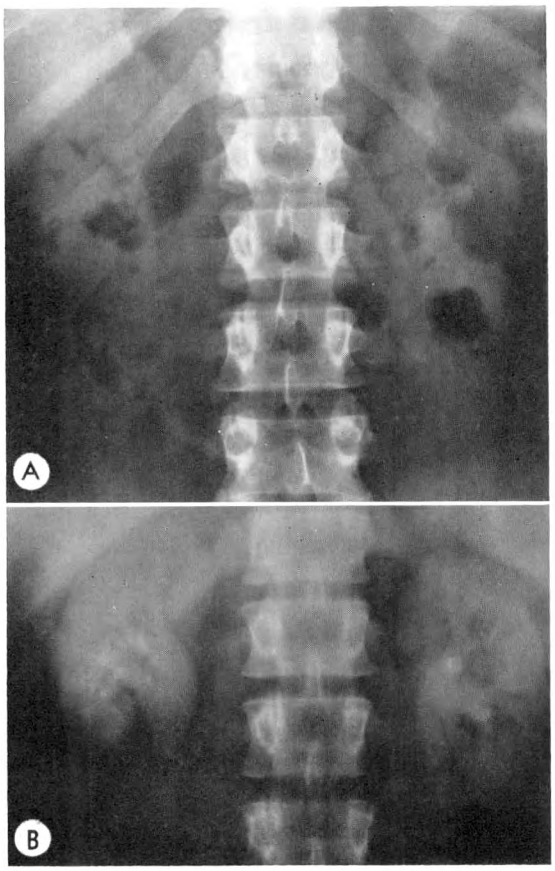


FIG. 2. A 25 year old man with proteinuria for 8 years and hypertension for 3 years. Chronic renal insufficiency secondary to glomerulonephritis. The serum creatinine was 4.4 mg./100 ml. and the creatinine clearance 17 ml./min./1.73 sq. m. (*A*) Conventional urogram with 30 ml. of contrast medium. (*B*) After immediate injection and tomography, giving a diagnostic study.

tions that were terminated, 1 patient with a serum creatinine of 11.3 mg./100 ml. and a creatinine clearance of 4.8 ml./min./1.73 sq. m. had multiple myeloma and a mass in the left kidney that was visible on the tomograms; the other patient had a serum creatinine value of 8.5 mg./100 ml. and the creatinine clearance was not determined. Urinary-tract obstruction could be excluded, however.

CONVENTIONAL UROGRAPHY PLUS REINJECTION

Immediate re-examination using a 50 ml. dose of hypaque-M, 90 per cent, was carried out in 12 urograms when the conventional dose of 30 ml. of contrast medium failed to adequately demonstrate renal anatomy urographically. Serum creatinine values ranged from 2.4 through 7.2 mg./100 ml. in these patients, and the creatinine clearance ranged from 10 through 30 ml./min./1.73 sq. m. in the 6 patients in whom it was done. With this added dose of contrast medium, the renal parenchyma was demonstrated satisfactorily in 12, the calyces in 10, and one or both ureters in 12 (Fig. 2, *A* and *B*). In only 2 cases were the calyces either poorly seen or not visualized by this supplementary injection; the serum creatinine values were 4.8 and 7.2 mg./100 ml., respectively, and the creatinine clearances were not done.

DRIP-INFUSION STUDIES

Of the 42 examinations done in 39 patients by the drip-infusion technique, urography demonstrated the renal cortex and the calyces well enough to be classified as good or satisfactory in 40 and 37 instances, respectively. In the 3 instances in which the calyces were not seen well, both ureters were demonstrated; thus, a surgically correctable obstructive lesion could be ruled out. The serum creatinine values ranged from 1.15 through 19.5 mg./100 ml. in these cases and the creatinine clearance in 38 cases ranged from 4.6 through 54 ml./min./1.73 sq. m. In only 2 patients was the examination by infusion less than satisfactory by the criteria outlined in Table 1. In 1 patient who had diabetic nephropathy, a serum creatinine value of 11.6 mg./100 ml., and a creatinine clearance of 3.4 ml./min./1.73 sq. m., the urogram showed parenchyma well enough to determine renal size and suggest chronicity of the disease. In the second patient who had renal impairment of undetermined cause, a serum creatinine value of 3.05 mg./100 ml., and benign prostatic hypertrophy, the urogram showed the renal parenchyma and ureters poorly but did confirm the absence of an obstructive process.

Table III

COMPARISON OF ANATOMIC VISUALIZATION WITH SERUM CREATININE VALUE

Serum Creatinine (mg./100 ml.)	Renal Parenchyma Visualized		Calyces Visualized		Ureter(s) Visualized	
	Yes	No	Yes	No	Yes	No
1.15– 2.9	21	0	21	0	20	1
3.0 – 4.9	21	1	20	2	20	2
5.0 – 6.9	11	1	9	3	11	1
7.0 –19.5	9	2	6	5	7	4

SERUM CREATININE AND ANATOMIC VISUALIZATION

Comparison of the degree of renal function impairment, as indicated by the serum creatinine value, with the quality of anatomic visualization of renal anatomy is summarized in Table III. The results of the examinations were divided, for convenience, into 4 categories on the basis of the serum creatinine values as previously outlined. The total range of serum creatinine values in the series was from 1.15 through 19.5 mg./100 ml.

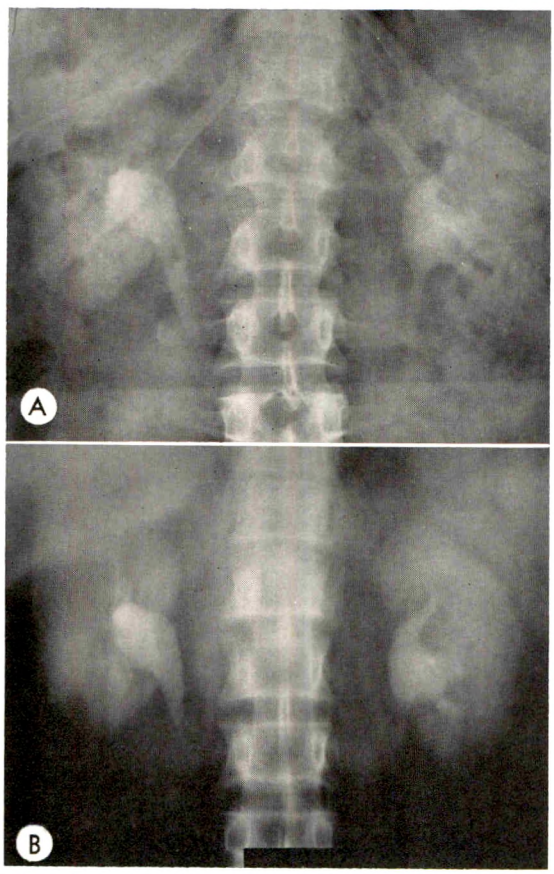


Fig. 3. A 46 year old man with recurrent urinary tract infections and recent onset of hypertension. Serum creatinine was 2.7 mg./100 ml. and the creatinine clearance 30 ml./min./1.73 sq. m. (*A*) Parenchyma and calyces are poorly demonstrated. (*B*) Unsuspected cyst was diagnosed in right kidney after reinjection and tomography.

1. *Serum creatinine values from 1.15 through 2.9 mg./100 ml. (21 examinations).* Of the 21 examinations in patients with serum clearance values from 1.15 through 2.9 mg./100 ml. and endogenous creatinine clearance values between 30 and 42 ml./min./1.73 sq. m., the renal parenchyma as well as the calyces and renal pelvis was demonstrated well enough to be classified as good or satisfactory in every case. One or both ureters were seen in 20 of the examinations (Fig. 3, *A* and *B*).

2. *Serum creatinine values from 3.0 through 4.9 mg./100 ml. (22 examinations).* Among 22 examinations done in patients whose serum creatinine values ranged from 3.0 through 4.9 mg./100 ml. and creatinine clearance values were from 15 through 34 ml./min./1.73 sq. m., the parenchyma was demonstrated in 21 and the calyces and one or both ureters in 20 instances (Fig. 4).

In 2 patients whose serum creatinine values were 3.75 mg./100 ml. and 4.8 mg./100 ml., respectively, the calyces and pelvis of the kidneys were poorly demonstrated, but opacification of the ureters, even though poor, made it possible to exclude a surgically correctable lesion such as obstruction.



FIG. 4. A 26 year old man with recurrent urinary tract infections since 2 months of age. He had been operated on in 1961 for megalo-ureter and right hydronephrosis. Serum creatinine was 3.4 mg./100 ml. and the creatinine clearance 33 ml./min./1.73 sq. m. An infusion study demonstrates only the shell of a functioning kidney with a large hydroureter and hydronephrosis on the left.

3. *Serum creatinine values from 5.0 through 6.9 mg./100 ml. (12 examinations).* Of the 12 examinations of patients with serum creatinine values from 5.0 through 6.9 mg./100 ml. and creatinine clearance values from 10 through 18 ml./min./1.73 sq. m., the parenchyma and one or both ureters were demonstrated satisfactorily 11 times. Calyceal detail was seen well enough for the studies to be included in our good or satisfactory categories in 9 instances (Fig. 5, *A* and *B*; and 6).

Of the 3 patients whose urograms did not satisfactorily demonstrate parenchyma and calyces, 1 patient was a 13 year old boy with chronic pyelonephritis and secondary renal osteodystrophy whose serum creatinine level was 6.8 mg./100 ml. and the creatinine clearance was 7.4 ml./min./1.73 sq. m. Another patient with chronic glomerulonephritis and serum creatinine of 5.67 mg./100 ml. had only 30 ml. of contrast medium and no tomography. The third was a patient with hydronephrosis, pyelonephritis, nonfunction of one kidney, and a serum creatinine level of 5.85 mg./100 ml. Even though the renal pelvis, calyces, and ureters were not opacified on one side in this third patient, the diagnosis of hydronephrosis was possible because of the characteristic crescent-sign appearance of hydronephrosis seen on the urogram.

4. *Serum creatinine values greater than 7.0 mg./100 ml. (11 examinations).* Serum creatinine values ranging from 7.0 through

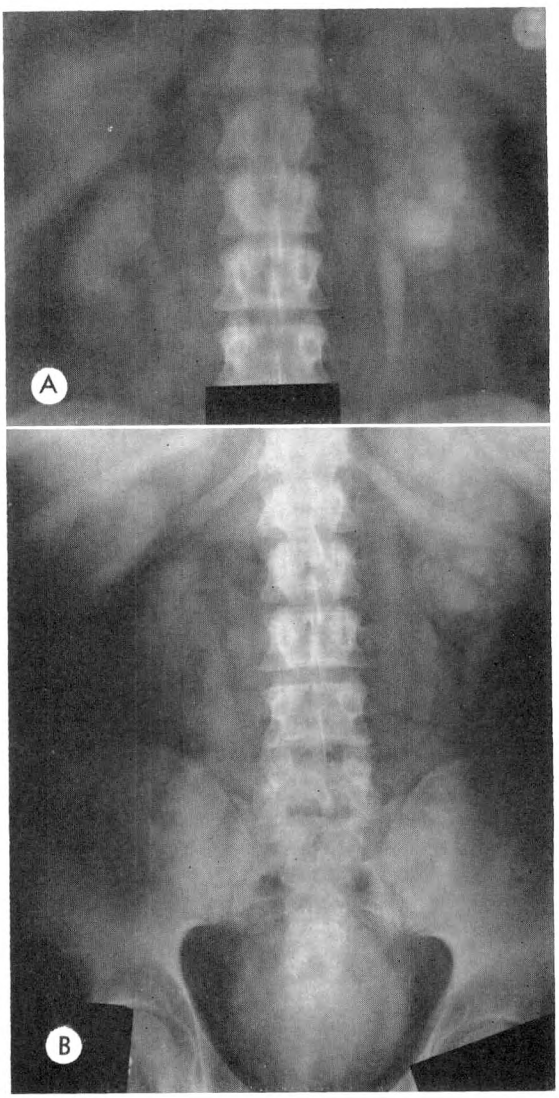


FIG. 5. A 22 year old man at age 4 years had a diagnosis of congenital absence of the abdominal musculature. He had chronic recurrent urinary tract infections with *Pseudomonas*. The serum creatinine was 5.15 mg./100 ml. and the creatinine clearance 19.9 ml./min./1.73 sq. m. (*A* and *B*) Reinjection and tomography demonstrate bilateral cortical scarring, pyelocaliectasis associated with pyelonephritis, and bilateral ureterectasis.

19.5 mg./100 ml. and creatinine clearances between 4.5 and 14 ml./min./1.73 sq. m. were obtained prior to examinations in 11 cases. The renal parenchyma was satisfactorily visualized in 9 of these cases (Fig. 7, *A* and *B*; and 8).

The 2 patients whose parenchyma did not visualize satisfactorily had poor calyceal and ureteral demonstration as well. The first patient, with hypertensive nephropathy and a serum creatinine level of 8.5 mg./100 ml., had a standard 30 ml. dose of contrast medium and no tomography. The second patient, with diabetic nephropathy and a serum creatinine level of 11.6 mg./100 ml., had the previously mentioned infusion study. In the remaining 3 patients in whom the calyces were not well seen, 1 patient, with a serum creatinine level of 7.2 mg./100 ml., did not have tomography. A second patient, with a serum creatinine level of 8.85 mg./100 ml., had adequate demonstration of the ureters, and extraurinary obstruction could be ruled out. The third patient, with a serum creatinine level of 11.3 mg./100 ml., had

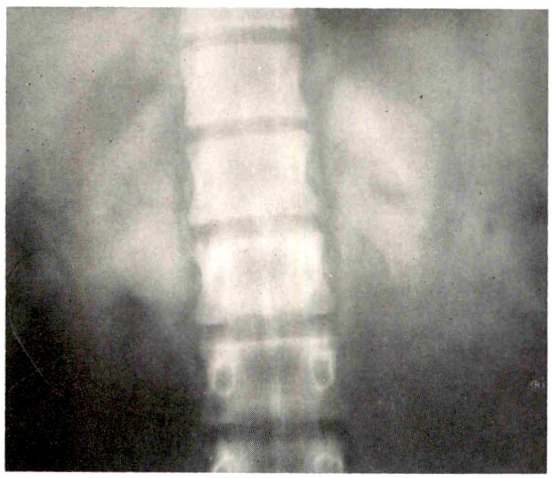


Fig. 6. A 14 year old girl with recurrent urinary tract infections since infancy. She had a recent onset of hypertension. Cystograms demonstrated bilateral ureteral vesicle reflux. Serum creatinine was 5.25 mg./100 ml. and the creatinine clearance 10 ml./min./1.73 sq. m. Reinjection and tomography demonstrate severe loss of renal cortex and pyelocaliectasis without obstruction.

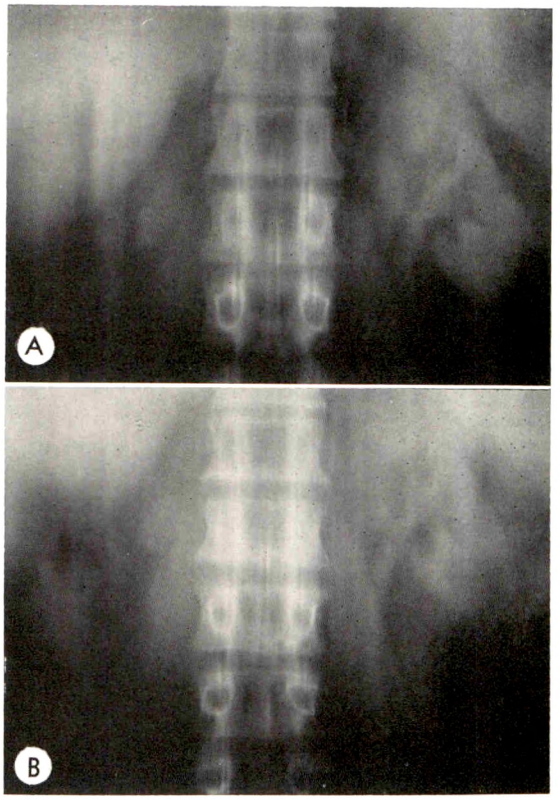


Fig. 7. A 56 year old man with recurrent urinary tract infections and pyelonephritis. Serum creatinine was 15.0 mg./100 ml. and the creatinine clearance 5.4 ml./min./1.73 sq. m. (*A*) Infusion study demonstrates atrophic, scarred, and nonfunctional right kidney. (*B*) Collecting system is demonstrated on the left to rule out ureteral obstruction.

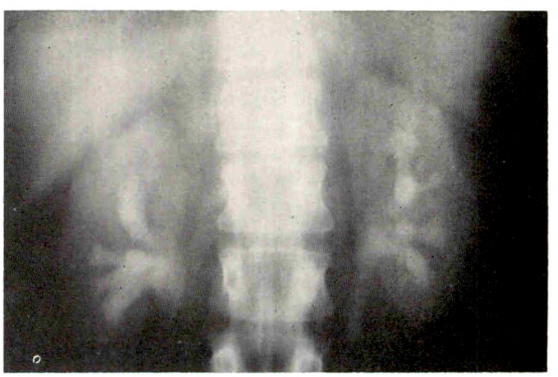


Fig. 8. A 43 year old woman had been a diabetic since she was 11 years old. She had pyelonephritis and renal insufficiency. The serum creatinine was 12.3 mg./100 ml. and the blood urea clearance 120 mg./100 ml. An infusion study demonstrates bilateral cortical scarring and pyelocaliectasis.

TABLE IV

SERUM CREATININE AND CREATININE CLEARANCE VALUES BEFORE AND AFTER UROGRAPHIC EXAMINATION

Case	Interval by Days	Serum Creatinine, (mg./100 ml.)		Change* (mg./100 ml.)	Creatinine Clearance, (ml./min./1.73 sq. m.)		Change† (mg./100 ml.)
		Before Urography	After Urography		Before Urography	After Urography	
1	1	2.40	2.15	+0.25	35.0	37.0	+2.0
2	3	5.67	5.25	+0.42			
3	1	6.90	6.75	+0.15	12.0	16.0	+4.0
4	4	2.85	3.35	−0.50			
	3	3.25	3.55	−0.30	29.0	32.0	+3.0
5	1	5.25	4.95	+0.30	10.0	18.0	+8.0
6	3	15.00	15.30	−0.30	5.4	5.0	+0.4
7	12	1.75	1.85	−0.10	30.0	25.0	−5.0
8	2	7.50	8.00	−0.50			
9	8	4.50	4.25	+0.25			
10	6	5.20	5.15	+0.05			
11	5	3.75	3.05	+0.70			
12	6	5.30	5.45	−0.15			
13	6	7.20	6.45	+0.75			
14	5	3.75	4.35	−0.60			
15	1	5.25	4.50	+0.75	15.0	18.0	+3.0
	1	4.50	4.90	−0.40	18.0	15.0	−3.0
16	1	12.50	11.60	+0.90			
17	3	2.05	2.15	−0.10	35.0	33.0	−2.0
18	2	15.00	14.90	+0.10	4.6	6.7	+2.1
19	6	1.15	0.90	+0.25	42.0	58.0	+16.0
20	1	3.05	3.25	−0.20	34.0	23.0	−11.0

* Plus (+) indicates decreasing; minus (−) indicates increasing.
† Plus (+) indicates increasing; minus (−) indicates decreasing.

multiple myeloma and an associated mass lesion that was demonstrable.

SERUM CREATININE AND CREATININE CLEARANCE VALUES BEFORE AND AFTER UROGRAPHY

Table IV lists the results of serum creatinine and endogenous creatinine clearance determinations made before and after urographic examinations in 20 patients from this series. After urography, a mean *decrease* of 0.08 mg./100 ml. in the serum creatinine concentration was demonstrated in these 20 patients who had 22 determinations of serum creatinine concentration prior to the intravenous examination. The values ranged from an increase of 0.6 mg./100 ml. to a decrease of 0.75 mg./100 ml.

Twelve determinations (1 patient had 2 separate examinations) of creatinine clearances before and after urography were obtained. These showed a mean *increase* of creatinine clearance of 1.3 ml./min./1.73 sq. m. The range of clearance values after the urographic study was from a decrease of 11.0 ml./min./1.73 sq. m. to an increase of 16.0 ml./min./1.73 sq. m. In both groups of determinations, the changes observed were within the expected range of error of the method and cannot be attributed to alterations in renal function by the examination.

DISCUSSION

Our experience indicates that excretory urography can be performed successfully in many or even most patients who have impaired renal function. The degree of opacification of the kidney and the clarity with which renal anatomy is demonstrated is obviously dependent, to a considerable degree, on the severity of the functional impairment; but it is also dependent, to

an equal degree, on the dose of the contrast medium and on the filming technique used for the examination.

Ross and associates,[11] using a dose of 50 to 60 ml. of 50 per cent hypaque, were unable to produce a truly satisfactory examination in any patient in whom the serum creatinine level was greater than 3.5 mg./100 ml. Even with laminagraphy, no useful study could be done when the serum creatinine level was greater than 5.5 mg./100 ml. Using the blood urea as an index of renal function, Scott[15] and Hartley[10] found that with doses as high as 80 ml. of 45 per cent hypaque, administered by a rapid intravenous infusion technique, diagnostically useful excretory urographic studies could be obtained only if the blood urea value was less than 120 mg./100 ml.

Schwartz and associates,[14] using what is now considered to be small amounts of urographic contrast medium (60 ml., renografin), showed that a satisfactory examination, with demonstration of the renal pelvis, could be obtained in patients with serum creatinine values as high as 12 mg./100 ml.; in their series, however, only 30 per cent had what they termed a satisfactory examination when the serum creatinine value was more than 5 mg./100 ml., and in only 5 per cent of the examinations were the calyces satisfactorily visualized, even with the adjunctive use of tomography.

Several authors[2,8,12,13] have suggested that the use of larger amounts of contrast medium gives the best demonstration of renal anatomy.

Doyle and associates,[6] in a controlled study employing doses of urografin 60 per cent ranging from 0.5 ml./kg. through 4 ml./kg. of body weight, found that 2 ml./kg. or its equivalent was the optimal dose in their patients with renal function impairment. Even with this large dosage, they believed that calyceal detail was rarely satisfactorily demonstrated if the glomerular filtration rate was less than 25 ml./min.

Our experience, using small or conventional doses of urographic medium and plain film roentgenography, was essentially the same as that of others. It is only in the unusual instance that satisfactory opacification of the urinary tract was obtained when the serum creatinine was greater than 3.5 mg./100 ml.

In contrast, with large doses of 50 to 100 ml. of hypaque-M, 90 per cent, given intravenously, by direct injection or by infusion and with the use of tomography, this series demonstrates that significant anatomic and pathologic information can be obtained in almost all patients without regard to the severity of renal function impairment. For example, opacification of the renal parenchyma and calyceal system that was classified as good or satisfactory was obtained in patients who had serum creatinine values ranging from 1.15 through 19.5 mg./100 ml. and creatinine clearance values from 4.6 to 54 ml./min./1.73 sq. m., with this large dose of contrast medium when conventional techniques failed. Even in the presence of a "nonfunctioning" kidney resulting either from renal cortical disease or from obstruction, large doses of contrast medium made it possible to opacify the remaining renal cortical substance and to determine the size, location, and many anatomic and pathologic characteristics of the kidney.

From the results of our experience there does not appear to be any definite correlation between the values for serum creatinine and the values for endogenous creatinine clearance and between the type and the quality of the examination that will best demonstrate the renal anatomy at the various levels of renal function impairment. The reason for the lack of correlation between serum creatinine value and the quality of the excretory urogram is only conjectural. It is well known, however, that a linear relationship between serum creatinine levels and endogenous creatinine clearance values does not exist.[5] Other factors such as urinary diluting and concentrating ability and adequacy of patient preparation are but a few of the many variables that may well contribute to this lack of consistency.

One of the major concerns is whether or not any deleterious effect on renal function is produced as a result of the administration of these large doses of contrast medium.

Using 1 ml./lb. of body weight of 50 per cent hypaque diluted with equal amounts of 5 per cent dextrose and water, Gup and associates[9] studied a series of 10 patients. These authors suggested that there was a trend toward a decrease in renal plasma flow and glomerular filtration rate with increasing doses of contrast media, but they could not determine any deleterious effects on renal function.

Bishop and associates,[3] using doses of 50 ml. of 90 per cent hypaque did not observe any adverse effects on renal function in their patients. Schwartz and associates,[14] in their well-documented study of 90 patients, found only 5 patients who had an unexplained increase in serum creatinine values with doses of as large as 60 ml. of 60 per cent renografin, and in all but 1 of these patients, the change was transient. Whitesel and Heller,[17] using an even larger dose of from 90 to 150 ml. of 50 per cent hypaque, failed to detect any evidence of further renal impairment.

Support is lent to these observations by our own data in 20 cases in which doses of 30 ml. of renovist were used in 3 cases, 50 ml. of hypaque-M, 90 per cent, in 3 cases, and 100 ml. of hypaque-M, 90 per cent, in 13 cases. In these 20 cases, no change was demonstrated in the mean or individual values of serum creatinine or endogenous creatinine clearance beyond those expected to be inherent within the error of the method, and in no case was any clinical evidence of further deterioration in renal function demonstrated.

The demonstration of the gross anatomy of the kidneys and their collecting system by urographic techniques, such as have been described, is assuming increasing importance in the management of patients with renal insufficiency. The availability of effective medical therapy for certain renal parenchymal diseases, newer techniques in urologic surgery, and the increasing use of kidney transplantation has created a need for a more thorough diagnostic approach to nephrologic and urologic problems that were not amenable to treatment in the past.

This study strongly supports the view that urographic techniques can demonstrate the gross anatomy of the renal and collecting systems without apparent hazard to patients with renal function impairment. The patients studied in this series, however, do not represent, necessarily, all examples of conditions in which this technique might provide useful information. A number of situations do confront clinicians and urologists wherein potentially useful information may be obtained with the previously described urographic techniques. Several of these possible indications are subsequently discussed.

The presence or absence of obstructive uropathy in an azotemic patient may be confirmed without resort to retrograde pyelography, a procedure not without hazard, particularly in the presence of urinary tract infection.

The detection and differentiation of renal mass lesions in the presence of renal function impairment becomes increasingly important with better understanding of the conservative management of chronic renal insufficiency and the availability of effective dialysis techniques.

Patients with renal failure of recent symptomatic onset who have grossly normal-appearing kidneys, urographically, not uncommonly have a potentially reversible parenchymal renal disease. Demonstration of kidney size and location is a prerequisite to the successful technique of renal biopsy, a procedure which has contributed significantly to the understanding and treatment of acute parenchymal renal disease.

Azotemia after ureteral diversion procedures may develop as a result of acute renal failure, anastomotic obstruction, or pooling of urine in the intestine. Very often, retrograde pyelographic studies are not possible in this situation. The treatment of each of

these causes is different and usually successful, providing the correct diagnosis is made. The ability of excretory urography to aid in the differential diagnosis in this situation is of considerable importance.

Clues to the cause of chronic renal insufficiency may sometimes be obtained if renal and calyceal detail can be demonstrated. Calyceal changes suggestive of papillary necrosis may aid in the diagnosis of such conditions as chronic acetophenetidin (phenacetin) abuse or sickle-cell renal disease. Occasionally, polycystic kidney disease may be demonstrated in patients who have normal renal size but renal insufficiency.

One of the criteria for acceptability as a suitable kidney transplant candidate is the presence of a normally functioning bladder and urethra. Demonstration of bilateral hydroureters and hydronephrosis by excretory urography in this type of patient with end-stage renal disease may indicate the need for further urologic evaluation to exclude a lower urinary tract abnormality.

No doubt, other conditions exist in which excretory urographic techniques may be of value. Certainly future advances in the management of patients with renal failure will add other indications for the use of the technique.

SUMMARY AND CONCLUSIONS

Sixty-six intravenous urographic examinations were done in 55 cases in an attempt to clarify (1) the relationships between the degree of renal function impairment and the ability to demonstrate renal anatomy and (2) to gather data on the effect of large doses of excretory urographic contrast medium on renal function.

Patients were considered to have impaired renal function if the serum creatinine level was greater than 1.15 mg./100 ml. or the endogenous creatinine clearance was less than 50 ml./min./1.73 sq. m.

Serum creatinine values ranged from 1.15 mg./100 ml. through 19.5 mg./100 ml., and the creatinine clearance determinations from 3.6 to 54 ml./min./1.73 sq. m.

Three roentgenographic techniques were employed to study these patients: (1) conventional urography utilizing 30 ml. of contrast medium (renovist) supplemented by tomography as needed; (2) reinjection with 50 ml. of hypaque-M, 90 per cent, if the conventional dose was not adequate; and (3) infusion technique using 100 ml. of hypaque-M, 90 per cent, either with or without an equal amount of diluent.

The renal parenchyma was demonstrated with enough clarity to evaluate renal size, cortical thickness, scarring, or the presence of intrarenal mass lesions on 62 urograms (94 per cent). The renal pelvis and calyces were opacified well enough to determine the presence or absence of calyceal blunting, destructive changes, filling defects, pyelocaliectasis, or distortion by an intrarenal mass lesion on 56 urograms (85 per cent). And, one or both ureters were opacified on 58 urograms (88 per cent). There was no urogram in which so little renal anatomy was displayed that renal size and location could not be determined or in which the presence of urinary tract obstruction went undetected. No direct relationship between the degree of functional impairment, as measured by the serum creatinine and creatinine clearance values, and the ability to opacify the kidneys was demonstrated.

In 22 examinations (16 of these utilized the drip-infusion technique), the true serum creatinine values or endogenous creatinine clearance (or both) were obtained before and after urography was done. The changes in values observed were within the expected range of error of the method and cannot be attributed to alterations in renal function by the examination.

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ARTERIOGRAPHY OF ADRENAL NEOPLASMS*

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A REVIEW of the literature concerning adrenal arteriography reveals a considerable volume of material in which many of the authors conclude that arteriography is dangerous,[3,10] limited,[5] or impossible.[9] The purpose of this paper is to present an arteriographic study of 30 patients with adrenal neoplasms all of which were histologically verified. This study demonstrates that arteriography, in our experience, has proved to be a reliable diagnostic procedure. No complications were encountered in this series despite that fact that 11 of the patients had pheochromocytomas.

METHOD

In each case the arteriographic study consisted of at least selective renal arteriography and aortography. Any abnormal vessels that were seen on the aortogram were also selectively catheterized. Often it was necessary to selectively catheterize more than one artery, as 9 of the neoplasms had at least a dual blood supply. Twenty-three tumors were supplied by the inferior adrenal arteries; 10 by the middle adrenal arteries; and 4 by branches of the celiac axis. Serial roentgenography was often helpful and frequently showed abnormal veins in the neoplasm.

In all cases of suspected pheochromocytoma, the blood pressure and electrocardiogram were continuously monitored.[6] Phentolamine was available for immediate intravenous injection, in case of a sudden rise of blood pressure, via an intravenous infusion of 5 per cent glucose and water which was started prior to, and maintained during, the entire procedure. The injection of 5 mg. of phentolamine was generally sufficient to control a sudden increase in blood pressure in the presence of pheochromocytoma. On occasion, it was necessary to give repeated injections of 5 mg. of phentolamine to maintain the blood pressure at reasonable levels.

TABLE I

DATA ON ARTERIOGRAPHY OF ADRENAL NEOPLASMS IN 30 PATIENTS

I. Pheochromocytoma		11
II. Adrenal carcinoma		11
Cushing's syndrome	2	
No syndrome	9	
III. Metastases or direct extension of neoplasms to the adrenal gland		4
IV. Benign adrenal cortical adenomas		4
Cushing's syndrome	3	
Primary hyperaldosteronism	1	
		30

MATERIAL

The data of 30 patients (21 men and 9 women) are listed in Table 1. Indications for arteriography consisted of hypertension, and clinical or urographic evidence of neoplasm. One patient had bilateral benign adrenal pheochromocytomas. Metastases to the adrenal gland were from retroperitoneal neoplasms in 2 cases, a bronchogenic carcinoma and a renal cell carcinoma from the contralateral kidney.

RESULTS

Preoperative arteriography established a diagnosis of adrenal neoplasm in 29 of the 30 patients. The arteriographic findings are listed in Table 11.

PHEOCHROMOCYTOMA

In 6 of the 11 patients with pheochromocytoma, a significant blood pressure ele-

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TABLE II

ARTERIOGRAPHIC MANIFESTATIONS OF ADRENAL NEOPLASMS

	Total	Highly Vascular Neoplasms	Displacement of Vessels and Organs	Arteriographic Evidence of Metastases	Blood Pressure Response
Pheochromocytoma	11*	10†	8	1‡	6
Primary malignant neoplasm	11	9	10	5	0
Metastases or direct extension to the adrenal gland	4	1	4		0
Adenomas	4	3	1	0	0

* Bilateral tumors were present in 1 case.
† No arteriograms were obtained in 1 case.
‡ One benign pheochromocytoma was reported as showing liver metastases (at surgery the tumor was adherent to, but did not invade the liver).

vation occurred during the course of arteriography. Ten patients each had at least one provocative test either before or after the arteriography. The following agents were used: histamine, glucagon, or tyramine. From these conventional provocative tests, a significant elevation in blood pressure was noted in 8 patients.

Arteriographically, pheochromocytomas were noted to be extremely vascular in 10 of the 11 patients (Fig. 1, *A* and *B*). No arteriograms were obtained in 1 case as small injections of contrast medium (1 ml.) into the right renal artery produced marked blood pressure elevation and was associated with arrhythmia.[6] It was considered unwise to obtain morphologic proof in this case, and the presence of pheochromocytoma was confirmed at surgery.

ADRENAL CARCINOMA

Primary malignant neoplasms of the adrenal gland were generally quite vascular (Fig. 2, *A*, *B* and *C*). Arteriovenous

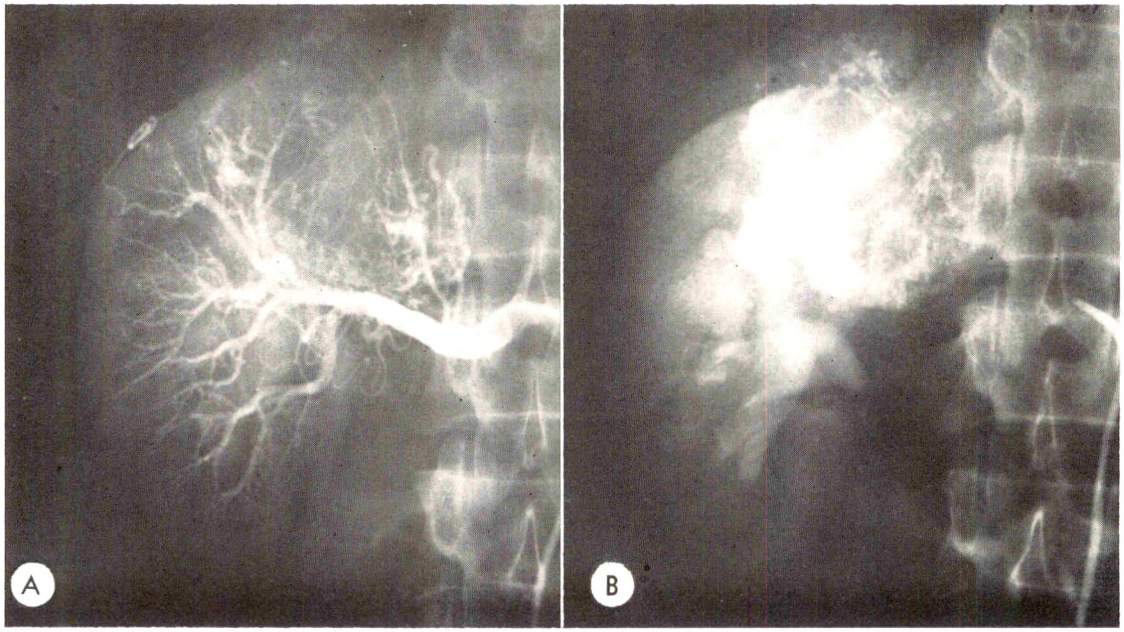


FIG. 1. (*A*) Mid arterial phase of a selective renal arteriography with numerous arteriovenous lakes, abnormal veins and dilated adrenal arteries. (*B*) Capillary phase showing more extensive filling of abnormal vessels in a benign pheochromocytoma.

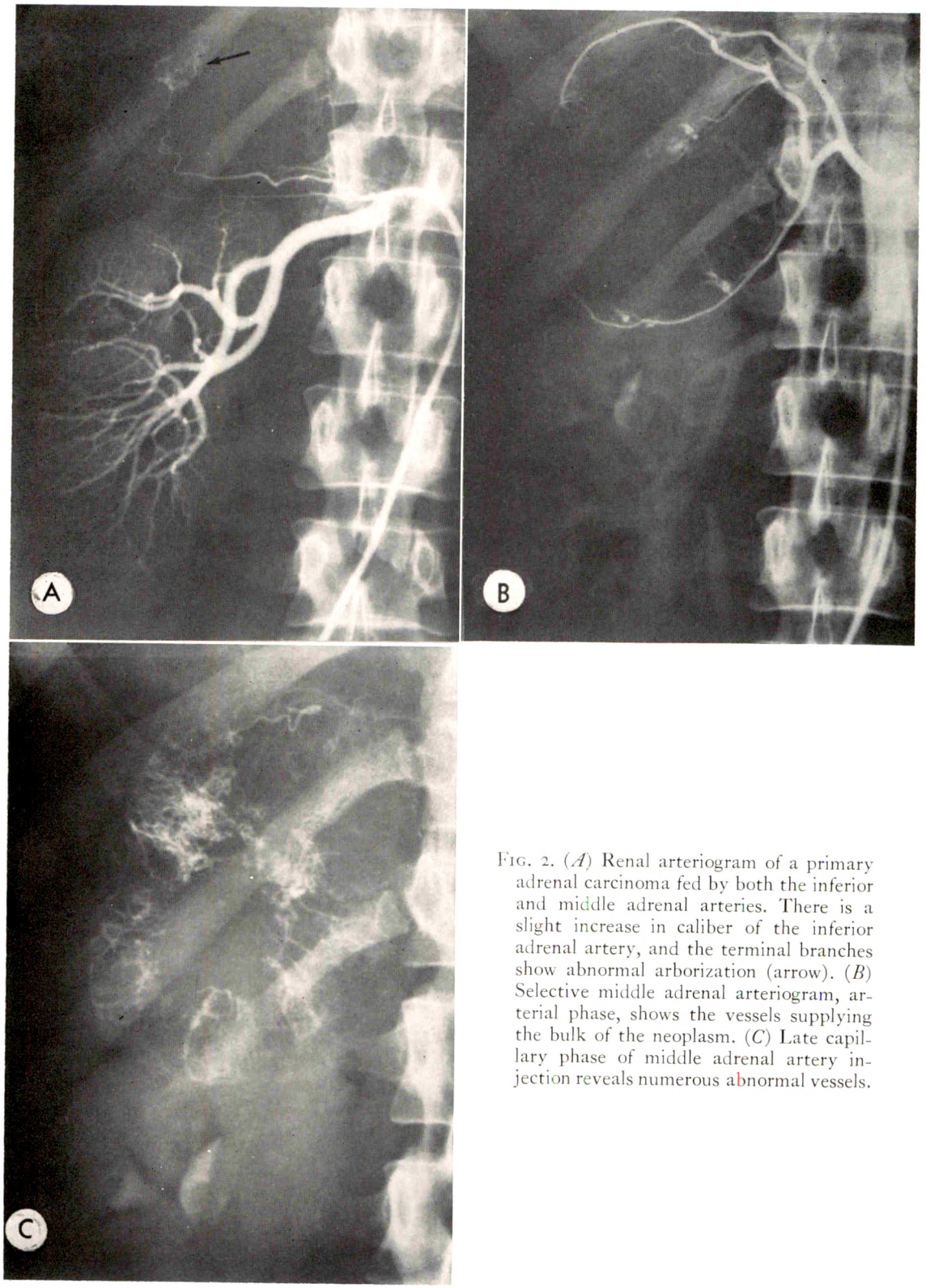


Fig. 2. (*A*) Renal arteriogram of a primary adrenal carcinoma fed by both the inferior and middle adrenal arteries. There is a slight increase in caliber of the inferior adrenal artery, and the terminal branches show abnormal arborization (arrow). (*B*) Selective middle adrenal arteriogram, arterial phase, shows the vessels supplying the bulk of the neoplasm. (*C*) Late capillary phase of middle adrenal artery injection reveals numerous abnormal vessels.

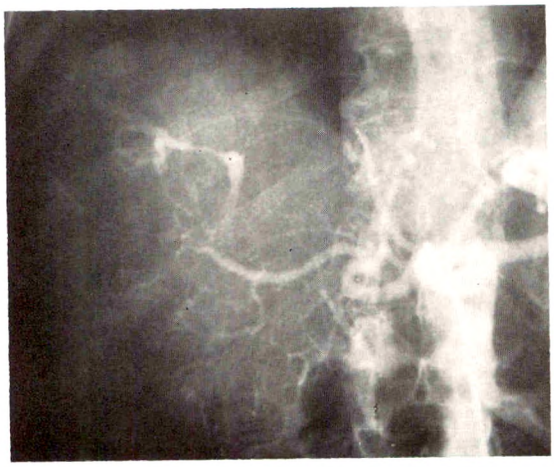


FIG. 3. Celiac arteriogram showing encasement of the hepatic artery and an arteriovenous communication produced by metastases from a primary adrenal carcinoma. (Reprinted by permission of *Radiology*, 1968, *90*, 1138.)

lakes were frequently seen and the adrenal veins were often partially visualized in the late arterial or capillary phase. It has become a routine in our department to study the liver by means of arteriography when an abdominal neoplasm is detected. In 5 of the 11 patients with primary adrenal carcinomas, hepatic metastases were detected by celiac arteriography performed in conjunction with the primary organ study (Fig. 3).

METASTATIC NEOPLASMS OF THE ADRENAL GLANDS

Our experience with metastatic neoplasms was limited to 4 cases. The majority were diagnosed by the presence of vessel or organ displacement and were relatively avascular. One metastasis was from a renal cell carcinoma of the contralateral kidney; like the primary tumor, it was quite vascular[1] (Fig. 4, *A* and *B*).

BENIGN ADENOMAS

Benign cortical adenomas were present in 4 patients; 3 had Cushing's syndrome, and 1 had primary aldosteronism. The arteriogram of 1 patient with Cushing's syndrome showed an extremely vascular

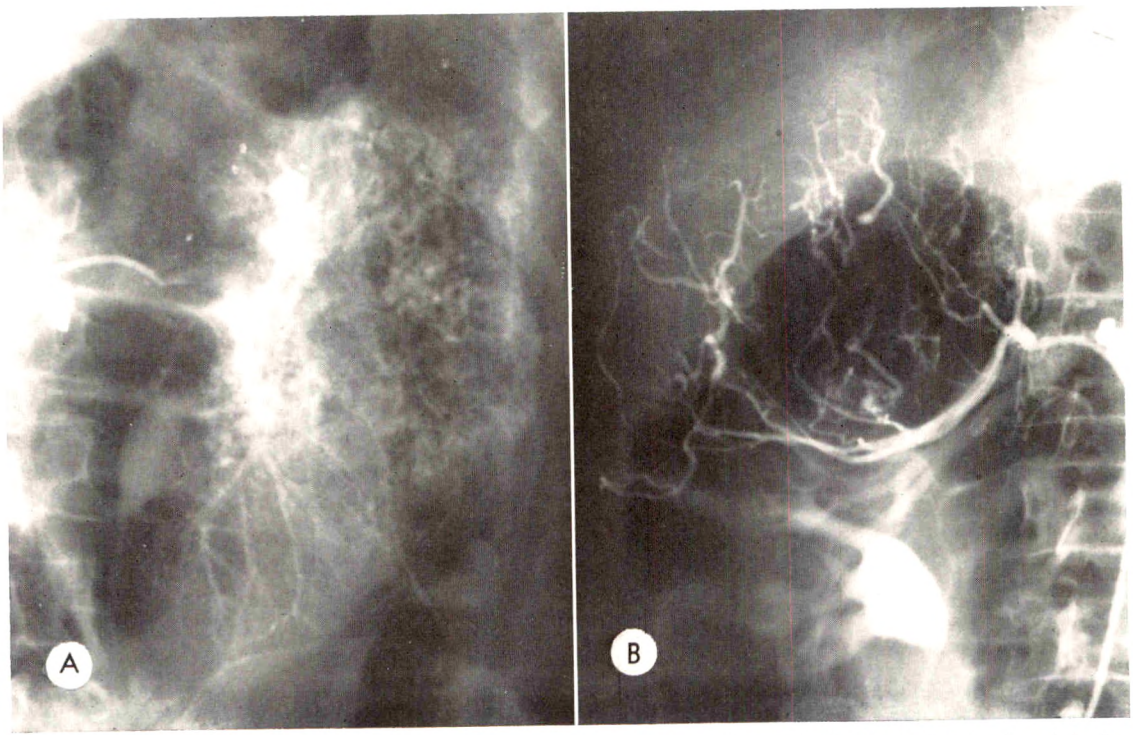


FIG. 4. (*A*) Selective renal arteriogram of a large primary renal carcinoma, left side. (*B*) Selective right inferior adrenal arteriogram (opposite side) demonstrates highly vascular metastasis from the contralateral renal carcinoma.

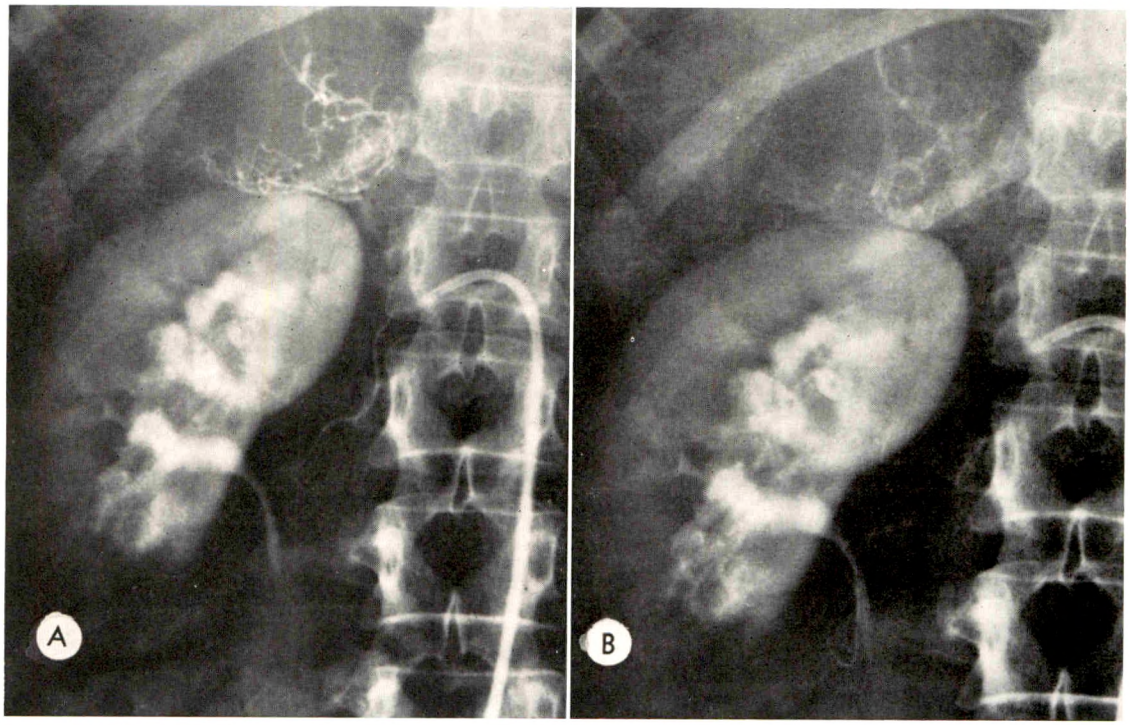


FIG. 5. (*A*) Late arterial phase of a selective right renal arteriography in a patient with Cushing's syndrome. Abnormal arborization and faint early venous filling of the large veins are demonstrated. (*B*) Large intra-adrenal veins in the venous phase of the arteriography. The lesion proved to be a benign cortical adenoma.

tumor with arteriovenous communication. This tumor appeared to be malignant (Fig. 5, *A* and *B*). Histologically, it proved to be a benign cortical adenoma. The other patients showed either a discrete blush or early venous filling in the region of the adenoma and slightly to moderately enlarged adrenal arteries.

DISCUSSION

The success of this study, in comparison with other reports, probably lies in the fact that selective and subselective arteriography was performed whenever possible. Selective renal or inferior adrenal arteriograms provided the majority of the diagnoses. Merklin and Michels,[8] in an extensive study of adrenal arterial anatomy, stated that: "The inferior suprarenal arteries are the most important, since they supply the thickest and largest part of the gland." This is in agreement with our results. In the majority of our patients the inferior adrenal artery was well visualized upon selective catheterization of the renal artery on either side. In several instances the aortogram demonstrated an enlarged and abnormal middle adrenal artery. In addition, selective celiac arteriography showed superior adrenal artery branches supplying the tumor in 4 cases (Fig. 6, *A* and *B*). We have concluded that a high aortography, with the catheter tip above the level of the celiac axis, and selective renal arteriography should be performed in the search for all adrenal neoplasms.

When a blood pressure response was not elicited in patients with pheochromocytoma, the arteriogram was frequently misinterpreted as showing a malignant neoplasm. All of the pheochromocytomas were benign upon histologic examination. In 1 case of pheochromocytoma, an extremely vascular tumor was demonstrated and no blood pressure response had been elicited. A celiac arteriogram showed evidence of

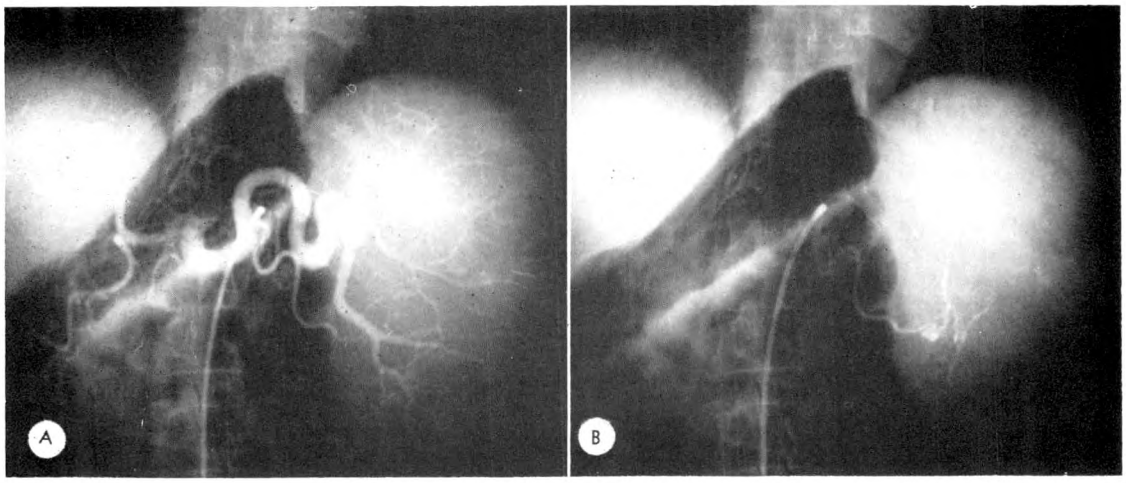


FIG. 6. (*A*) Early arterial phase of a celiac arteriography demonstrates a left superior adrenal artery emanating from the celiac axis. (*B*) Late arterial phase shows abnormal arborization within the tumor.

hepatic artery displacement and tumor staining in the lower margin of the liver. At operation the pheochromocytoma was adherent to the liver but was not invasive.

Adrenal phlebograms and retroperitoneal pneumograms were performed in too few patients to make a valid comparison. We do believe, however, that arteriography is associated with less discomfort than retroperitoneal pneumography. Arteriography has the added advantage of being able to demonstrate metastases to other abdominal viscera, when compared with adrenal venography and retroperitoneal pneumography.

Aldosterone producing adenomas of the adrenal gland are often small and it is doubtful that arteriography will consistently demonstrate lesions smaller than 1 cm. in diameter. We arteriographically

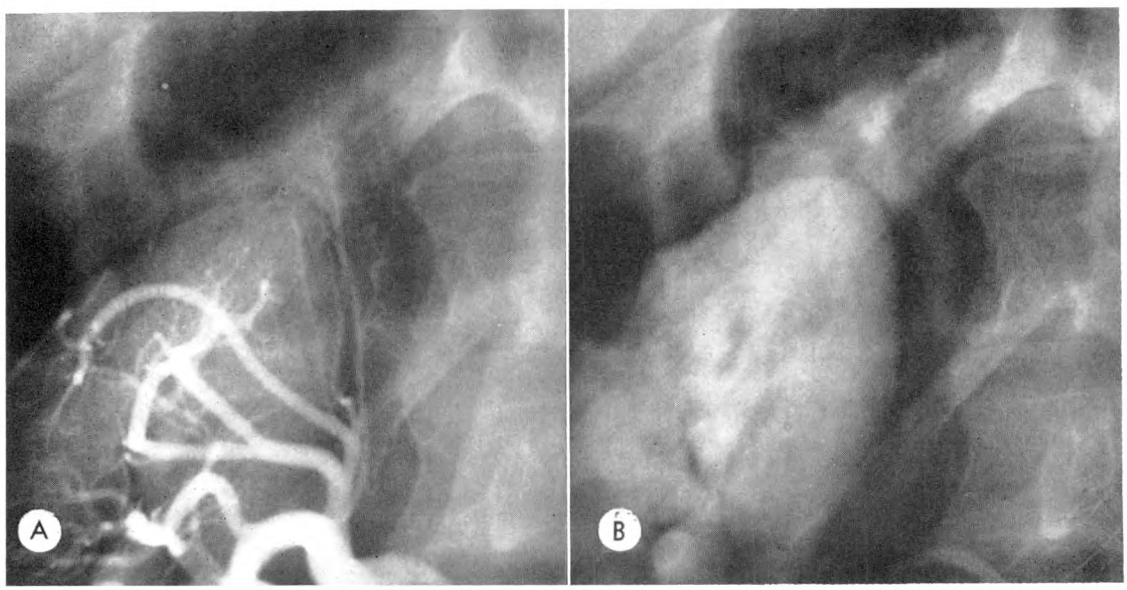


FIG. 7. (*A*) Arterial phase of a selective renal arteriography shows slight increase in the diameter of the inferior adrenal arteries. (*B*) Densely opacified adrenal adenoma, capillary phase. The adenoma was associated with primary hyperaldosteronism.

Table III

DIAGNOSTIC ACCURACY OF ARTERIOGRAPHY IN 30 CASES OF ADRENAL NEOPLASMS

Neoplasms	Total	Suspected Clinically	Evidence of Mass on Urogram	Correct Preoperative Arteriographic Diagnosis
Pheochromocytoma	11	9	4	10
Adrenal carcinoma and metastases to the adrenal gland	15	6	11	15
Adenoma	4	4	1	4
Total	30	19	16	29

detected one adenoma 9 mm. in diameter (Fig. 7, *A* and *B*), and Kahn[4] reported one that was slightly larger.

Adrenal phlebography in conjunction with adrenal venous blood sampling has been reported as a reliable method in the diagnosis of primary aldosteronism.[9] Unfortunately, hematomas of the adrenal gland have been produced by this method, and recently Bookstein and his associates[2] stated that adrenal venography cannot be recommended in the evaluation of primary aldosteronism.

SUMMARY

In contrast to numerous previous reports, we have found that adrenal arteriography has proved to be a remarkably accurate diagnostic procedure in the detection of adrenal neoplasms (Table III). The accuracy of this method is related to the fact that aortography was supplemented by at least selective renal arteriography. In several cases, selective arteriography of the celiac and middle adrenal arteries was necessary to demonstrate the tumor. In 5 patients, celiac arteriography performed in conjunction with adrenal arteriography showed liver metastasis from adrenal tumors.

We must conclude that arteriography of the adrenal gland is a safe and accurate procedure and that it provides more morphologic information than can be gained from conventional or other roentgenographic special procedures.

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ROENTGEN FINDINGS IN PSEUDOXANTHOMA ELASTICUM (PXE)*

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PSEUDOXANTHOMA elasticum (PXE) is a hereditary systemic disorder characterized by degeneration of elastic tissue. This condition was first described as an atypical xanthoma by Rigal in 1881 and it was not until many years later that the systemic nature of PXE was recognized. PXE is transmitted by a recessive gene that may be partially sex-linked.[1] The underlying defect has been shown to involve granulofilamentous material that forms the elastica and is first manifested by calcification and structural re-arrangement.[2,5,8,12] Since calcification appears to be primary and no "elastotic degeneration" of elastic tissue is seen, it has been suggested that a more appropriate term would be elastodysplasia calcificans.

Although an uncommon disease entity, the number of cases of PXE seems to be multiplying with awareness of this disorder. Between 1938 and 1951, 74 cases of pathologically proved PXE were seen at the Mayo Clinic.[2] Because no description of this disorder could be found in the roentgenologic literature, the authors analyzed cases from three large medical institutions and selected those which had undergone general roentgenologic study (19) in order to present the more characteristic findings.

CLINICAL SIGNS AND SYMPTOMS

PXE involves many organ systems and has protean manifestations. The most common clinical presentations are xanthoma-like skin lesions, upper gastrointestinal hemorrhage, and deterioration of visual acuity.[7]

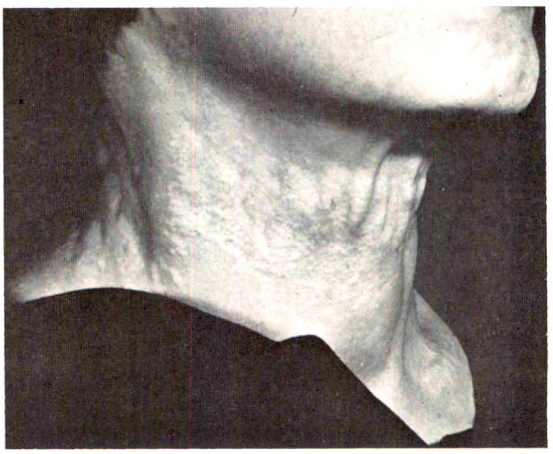


FIG. 1. The neck shows redundant folds of lax skin and "pseudoxanthomatous" yellowish papules.

DERMATOLOGIC FINDINGS

The most common sites of skin involvement are the neck and axillae where redundant folds of lax skin with "pseudoxanthomatous" yellowish papules, simulating Moroccan leather or the skin of a "plucked chicken," are noted (Fig. 1).[5] On the inner surface of the lip, clusters of small yellowish intramucosal nodules on a background of numerous dilated capillaries may be seen. The histologic changes of the skin appear to be confined to the middle and lower third of the dermis where the elastic fibers show curling, fragmentation, and calcification.[3] No normal elastic units are found in areas of involvement, and

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abnormal microscopic changes may be seen in areas of skin that are clinically normal. The onset of dermatologic manifestations is frequently in childhood.

OPHTHALMOLOGIC FEATURES

Many patients complain of diminished visual acuity due to marked alterations of the chorioretinal structures of the eye. Angioid streaks, reddish-brown serrated lines that extend from the optic disk in a spoke-like fashion (Fig. 2), are present in approximately 85 per cent of patients with PXE.[13] These angioid streaks are caused by linear separations in the outer portion of the lamina vitrea (Bruch's membrane) which is composed of elastic fibers. The appearance of the angioid streaks has been likened to "cracks in a dry lake bottom." Involvement of the macula in this degenerative process can lead to severe visual disability.[5,11]

VASCULAR MANIFESTATIONS

Gastrointestinal hemorrhage is not an uncommon manifestation of PXE and most often occurs in afflicted women during pregnancy. Gastroscopy shows a distinctive yellow cobblestone pattern of the mucosa resembling the cutaneous and buccal mucosal lesions. A similar appearance of the colonic mucosa has been found on sigmoidoscopic examination. Marked dilatation of mucosal and submucosal capillaries and veins with microaneurysm formation has been reported on microscopic study. These findings correlate with vascular dilatation and diffuse oozing noted gastroscopically with upper gastrointestinal hemorrhage in PXE.

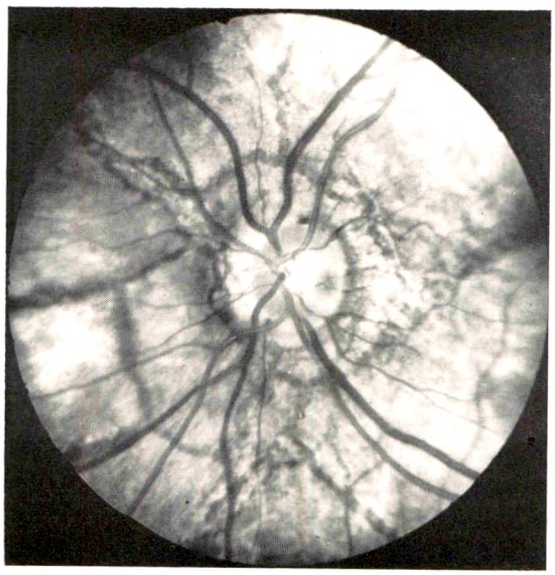


Fig. 2. Photograph of the optic fundus shows the characteristic serrated "angioid streaks" radiating from the optic disk.

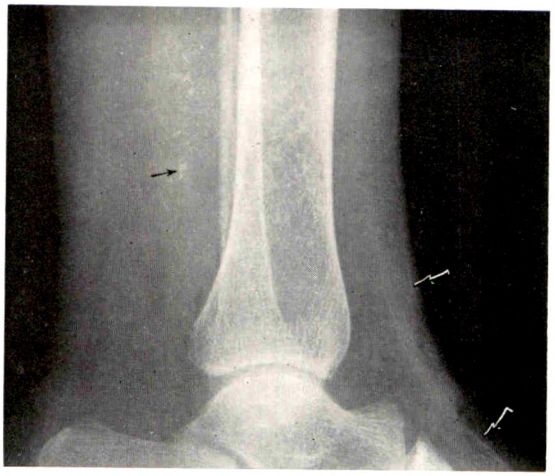


Fig. 3. "Calcinosis cutis" in deeper layers of dermis on dorsum of foot, and vascular calcification posteriorly in lower leg (arrows).

Intermittent claudication and diminished pulses in the extremities of children and young adults are common observations.[14] Microscopically, there is elastic tissue degeneration in the internal elastic lamina of the arteries. The diminished pulses may be caused by obstruction of medium-sized arteries by swollen, calcified medial tissue or by diminished transmission of the pulse wave by the vascular wall secondary to elastic tissue alterations.[19] The significant feature is not the occurrence of claudication and diminished pulses by themselves but the young age group in which they may be seen.

ROENTGENOLOGIC FINDINGS

SOFT TISSUE AND VASCULAR CALCIFICATION

The middle and deeper layers of the dermis are the usual areas of cutaneous



FIG. 4. Soft tissue calcification posteromedially in elbow.

calcification ("calcinosis cutis") (Fig. 3). Roentgenologically, calcification is more easily demonstrated in the extremities than in the trunk. The findings of extensive juxta-articular and soft tissue calcification in PXE have only recently been described.[9] These large amorphous calcium conglomerates are most commonly found at the elbow (Fig. 4), hip, and phalangeal areas. These "tumors" of calcification must be clinically differentiated from those found following trauma, in vitamin D overdosage, milk alkali syndrome, scleroderma, secondary hyperparathyroidism, or other less commonly encountered disorders.

In arteries both the intima and media are sites of calcification. Medial calcification is distributed fairly uniformly, whereas intimal calcification appears irregular, as sharply delimited plaques. Large veins may also have detectable mural calcification (Fig. 5).

The premature vascular calcification characteristically involves both upper and lower extremities. In the upper extremity, arterial disease is usually secondary to fibrous proliferation in the media. The arteriographic finding in either the radial or ulnar arteries is occlusion with marked collateral circulation (Fig. 6, *A* and *B*). Diminished flow to individual fingers may be present (Fig. 6*C*). Because of the diminished blood supply, soft tissue and osseous changes have also been seen in the form of ischemic resorption of the terminal phalangeal tufts (Fig. 7).

The vascular changes in the lower extremities are predominantly atherosclerotic and are seen as narrowing and irregularity of the abdominal aorta and more peripheral vessels. Femoral artery calcification occurs most commonly and has been observed as early as 9 years of age. Atherosclerotic plaques and occlusion of the superficial femoral artery (Fig. 8) are also seen in young patients.

OTHER MANIFESTATIONS

Various cardiovascular abnormalities, including aortic dilatation (Fig. 9) with



FIG. 5. Visualization of basilic vein probably due to mural calcification (arrows).

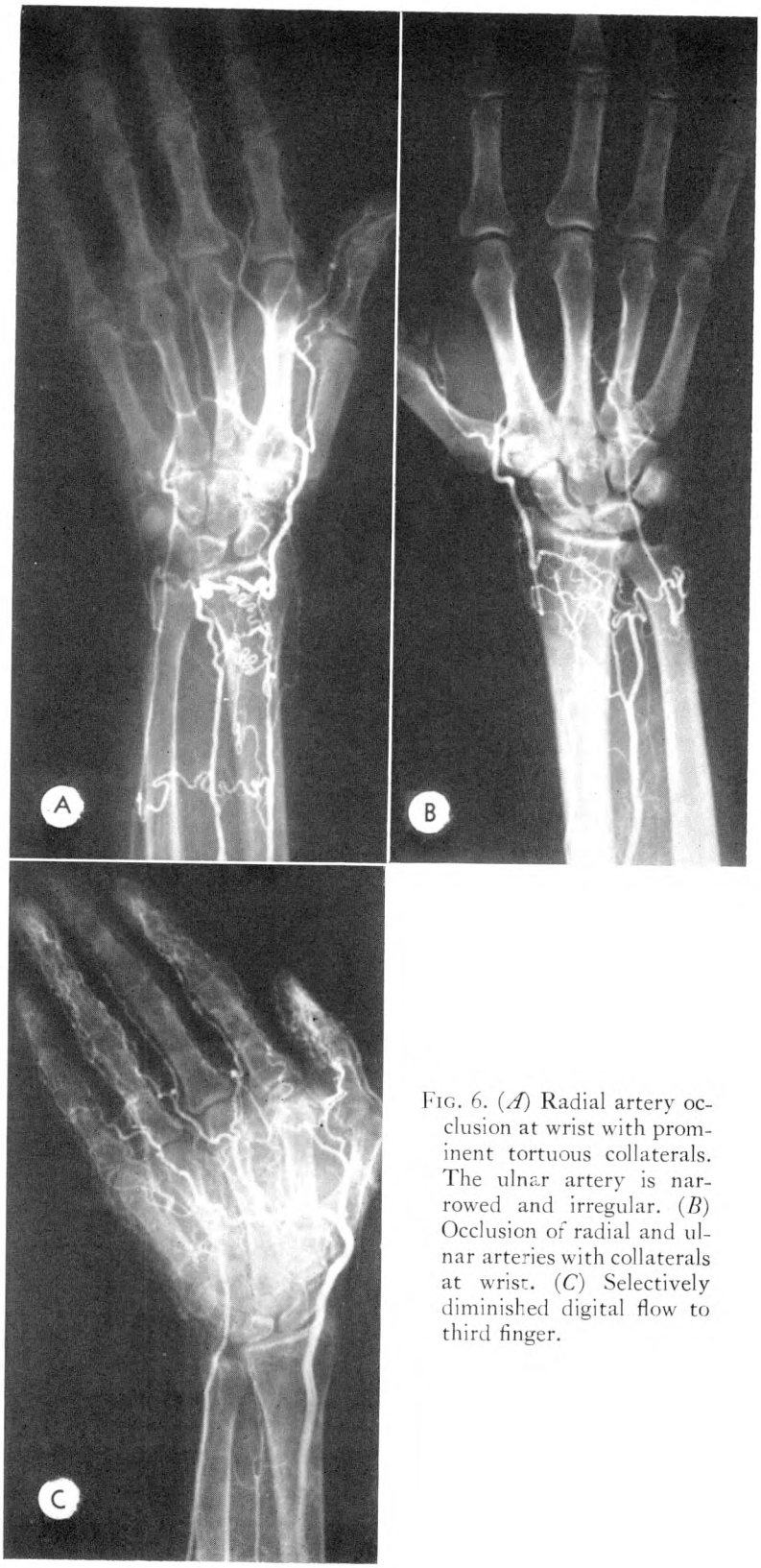


Fig. 6. (*A*) Radial artery occlusion at wrist with prominent tortuous collaterals. The ulnar artery is narrowed and irregular. (*B*) Occlusion of radial and ulnar arteries with collaterals at wrist. (*C*) Selectively diminished digital flow to third finger.



FIG. 7. Destruction of distal phalangeal tufts secondary to decreased vascularity (distal phalanx of fourth digit has been surgically amputated).

aneurysm formation and left ventricular hypertrophy secondary to hypertension, have been reported.[10,11]

If the upper gastrointestinal hemorrhage is investigated by a roentgen contrast examination of the upper gastrointestinal tract, a duodenal ulcer is sometimes found as the cause, but usually the examination is normal. A fine serrated appearance of the mucosa of the stomach occasionally correlates with the yellowish "cobblestone" mucosa observed gastroscopically (Fig. 10).[5]

The roentgenologic findings in pseudoxanthoma elasticum are widespread and varied. It is important for the roentgenologist to be aware of this disease entity and its roentgenologic manifestations in



FIG. 8. Tortuous collateral vessels secondary to superficial femoral artery occlusion.

order to suggest it as a possible diagnosis. However, for a definitive diagnosis, clinical correlation and pathologic proof are always necessary.

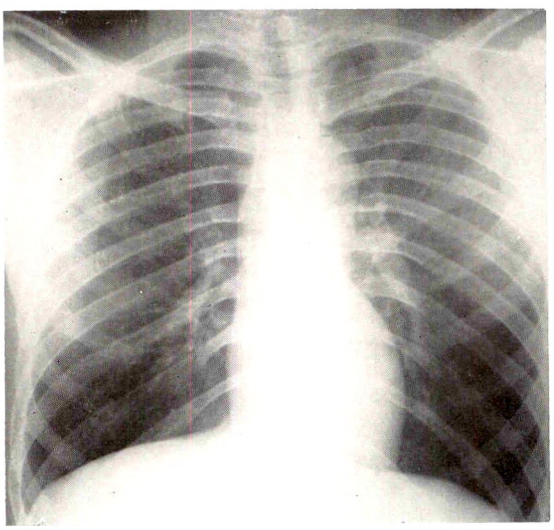


FIG. 9. Aortic dilatation in a 23 year old man with pseudoxanthoma elasticum (PXE).

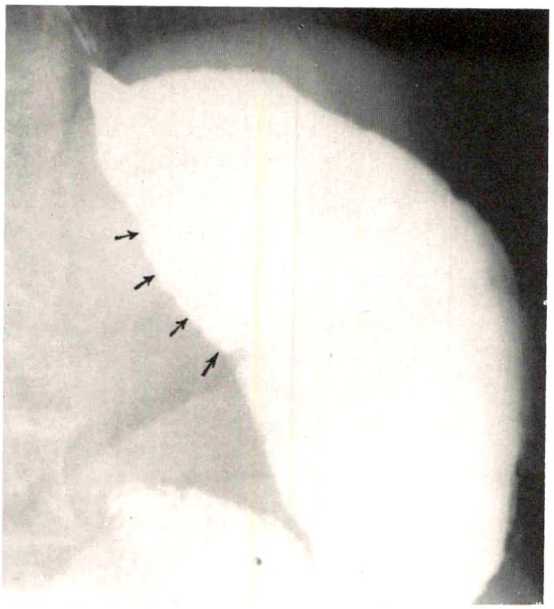


Fig. 10. Serrated appearance of the lesser curvature of fundus of the stomach (arrows).

SUMMARY

Pseudoxanthoma elasticum (PXE) is a systemic disorder characterized by xanthoma-like skin lesions, angioid streaks in the optic fundus, and gastrointestinal hemorrhage. This disorder is transmitted by an autosomal recessive gene and may represent a basic defect of calcium metabolism resulting in primary calcification of elastic tissue. The most common roentgenologic manifestations are soft tissue and vascular calcifications, atheromatous plaques, and narrowing of peripheral arteries. These roentgenologic features must be correlated with the clinical and pathologic findings.

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A SEMI-AUTOMATIC VACUUM CHEST UNIT*

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THE difficulties and inconvenience of handling 14×17 inch roentgenographic cassettes for large volume chest roentgenography are well known. The major drawback of the roentgenographic cassette, however, is imperfect screen contact, particularly in spring and fall due to warping to the bakelite front plate by changing humidity. It is the purpose of this communication to present a simple semi-automatic unit which closes intensifying screens by vacuum, thus achieving perfect contact.

METHOD AND MATERIAL

Up to sixty 14×17 inch films can be placed into magazine A (Fig. 1). The film is picked up by the vacuum lever B and transported to the left where it falls through a slot between the intensifying screens. By turning lever C, the intensifying screens are closed by the vacuum line D. Following completion of the exposure, the screens are opened and the film falls into the receiving magazine E. This magazine is small enough to be put in a standard

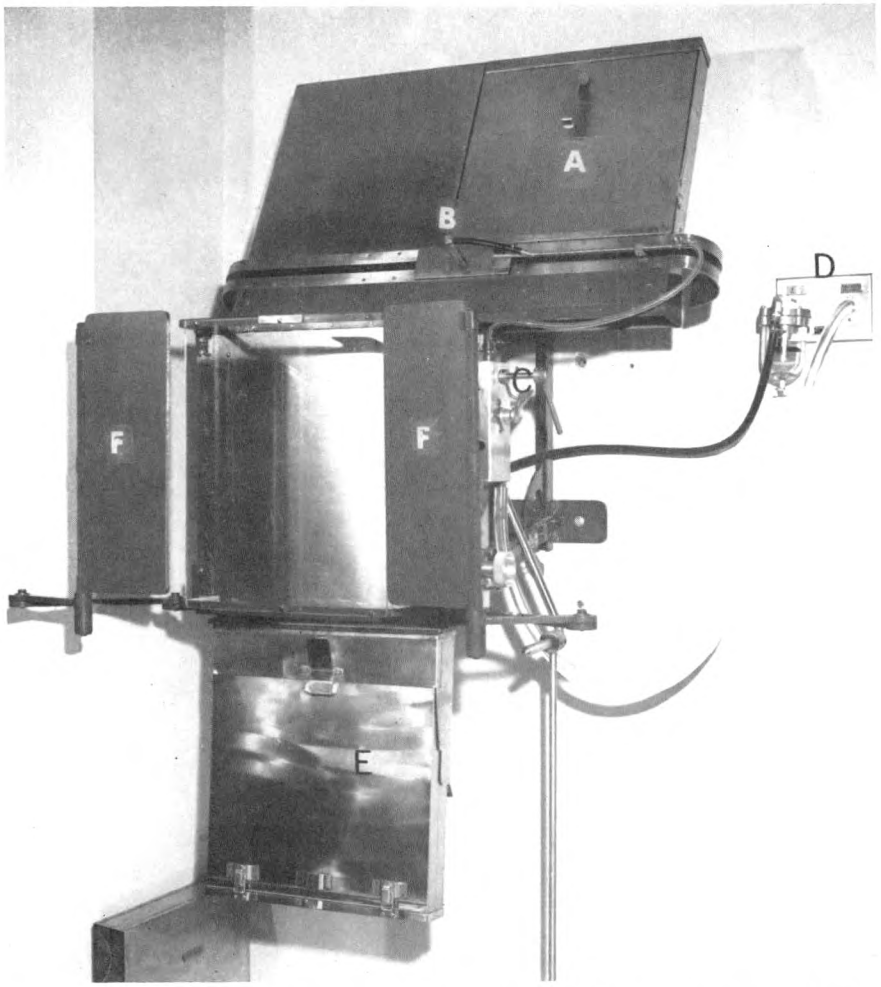


FIG. 1. Semi-automatic chest vacuum unit. A = magazine; B = lever (vacuum); C = lever; D = vacuum line; E = receiving magazine; F = flaps.

* From the Department of Radiology, University of Minnesota Hospitals, Minneapolis, Minnesota.

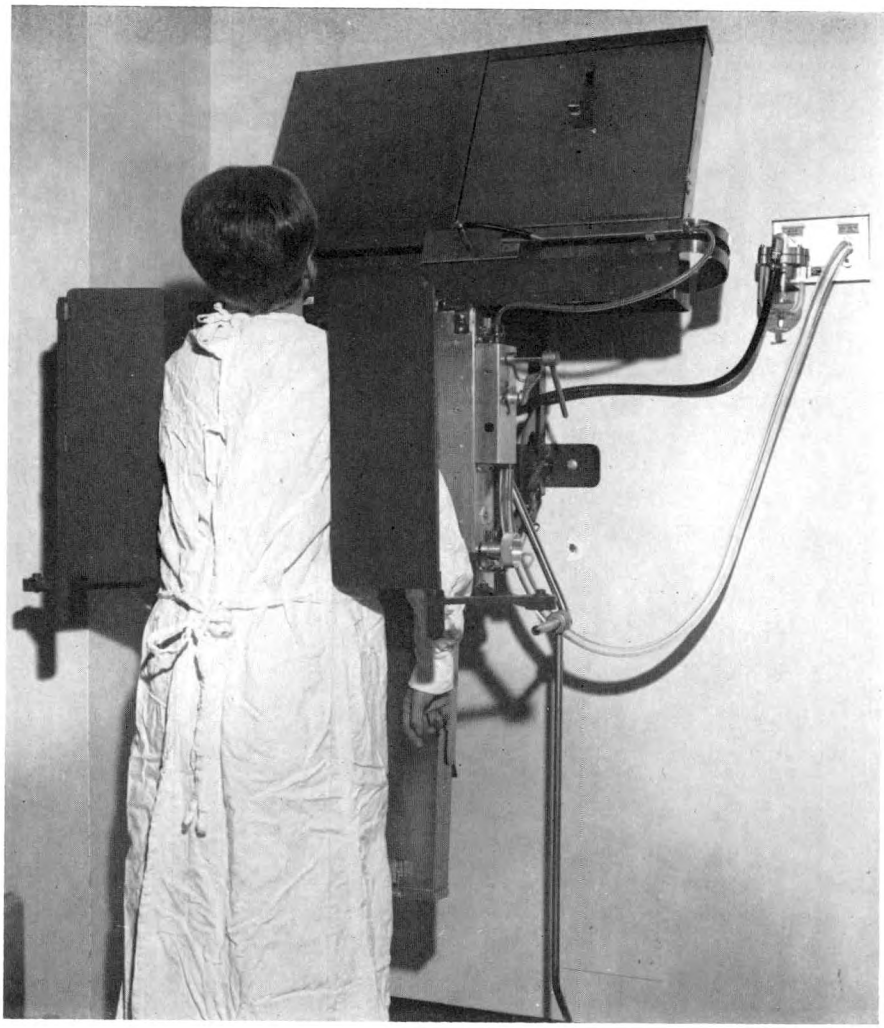


FIG. 2. Head flaps minimize secondary radiation and help achieve maximal coning. The flaps also aid in immobilizing the patient.

sized pass box for processing of films in the dark room. The height of the entire unit is easily adjustable by a spring balanced system.

For visualization of the heart and pulmonary vasculature a 150 kv. technique is used. To minimize secondary radiation an air gap of 3 inches is employed and maximal coning is achieved by lead flaps F. These flaps also help to immobilize the patient (Fig. 2).

DISCUSSION

The described unit is of extremely simple mechanical design and uses the hospital vacuum line as an effective means of obtaining screen contact. Since the intensifying screens are never touched by human hands and the system is closed and virtually dust free, the pair of screens should have an almost unlimited life and should not require frequent cleaning as is necessary with roentgenographic cassettes. Electric power is not necessary and screen contact is invariably perfect.

CONCLUSION AND SUMMARY

A simple vacuum device is described for chest roentgenography using the vacuum line of the hospital in order to achieve perfect screen contact. The unit is particularly helpful in large volume chest and heart roentgenography.

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SOME ASPECTS OF THE SQUARE WAVE RESPONSE FUNCTION OF RADIOGRAPHIC SCREEN-FILM SYSTEMS*

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IN THE past several years, considerable effort has been directed towards the measurement of the line spread-function (LSF) and modulation transfer function (MTF) of fluorescent screen-film systems used in medical radiography.

The LSF is defined as the relative spatial illuminance distribution in the image of a narrow slit. For a radiographic screen-film system, the LSF can be obtained by exciting the system with a narrow beam or "line" of x rays formed by a slit.[4,6,8,9] The slit used in this laboratory is approximately 12 microns wide and is formed by platinum jaws, 2 mm. thick.

The MTF is measured indirectly by computing it from the LSF by Fourier transformation. Figure 1 gives the LSF and MTF of Kodak Blue Brand Medical X-ray Film (ESTAR Base) exposed with medium-speed screens. An alternative method of obtaining the MTF is to use a square wave x-ray input to the screen-film system. The conversion of the square wave response function (SWRF) to the MTF has been discussed by Coltman[1] and also by Wittmann and Röhler.[10]

Of course, it would be desirable to obtain the MTF of a radiographic image-forming system directly by means of an x-ray pattern in which the irradiance distribution varies sinusoidally with distance. Unfortunately, it is difficult to produce a test object which transmits x rays in a sinusoidal fashion. Although the MTF is more fundamental than the SWRF, the SWRF itself appears to be a convenient means for assessing the light diffusion characteristics of screen-film systems. Some aspects of the SWRF will be investigated in this paper.

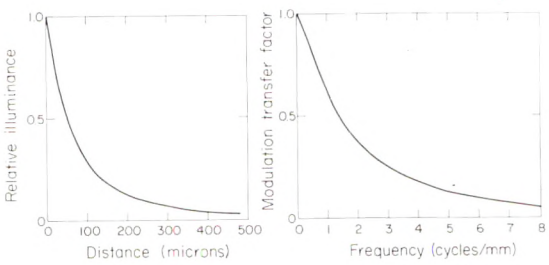


FIG. 1. Line spread-function (*left*) and modulation transfer function (*right*) of a screen-film system consisting of Kodak Blue Brand Medical X-ray Film (ESTAR Base) and 2 medium-speed screens.

SQUARE WAVE RESPONSE FUNCTION

A lead bar pattern* was used to obtain a spatial square wave x-ray input. The lead bar test object is made from lead 80 microns thick, and consists of a series of frequency† blocks. Each block is 1 cm. wide and consists of a series of parallel, equally spaced lead bars 1 cm. long. The spacing between the bars is the same as the width of the bars. The test object covers a frequency range of 0–5 line pairs/mm. in increments of 0.5 line pairs/mm. The zero frequency is obtained from large areas in the test object. A photographic reproduction of an image formed by the square wave test object is shown in Figure 2. The original image was recorded by direct x-ray exposure on Kodak Industrial X-ray Film, Type R (ESTAR Base) (Single-Coated).

To evaluate the SWRF of a screen-film system, a roentgenogram of the lead bar pattern is made. Subsequently, the density

* The test object was constructed by Herr E. Funk, Optiker, Am Hugenottenplatz 852, Erlangen, West Germany.

† The fundamental frequency of a spatial square wave pattern is numerically the same as the number of line pairs/mm.—not lines/mm. It is also equal to the reciprocal of the period of the square wave pattern.

* From the Research Laboratories, Eastman Kodak Company, Rochester, New York.

patterns on the film are measured with a scanning microdensitometer and the densities related to relative exposures by conventional photographic photometry (widestep sensitometry). However, widestep sensitometry can be used in this way with square wave images only if development effects (Eberhard effect) are not present in the emulsions.[5] If development effects were present, the SWRF would depend on the density level to which the film is exposed.

The SWRF of the screen-film system is defined as

$$\text{SWRF} = \frac{E_{\max} - E_{\min}}{E_{\max} + E_{\min}}, \qquad (1)$$

where $E_{\max}$ and $E_{\min}$ are the maximum and minimum exposures determined by photographic photometry of the film. Equation 1 is the ratio of the amplitude of the exposure deviation to the mean exposure. Although not indicated, $E_{\max}$ and $E_{\min}$ are functions of spatial frequency. For convenience, the SWRF is normalized to unity at zero spatial frequency.

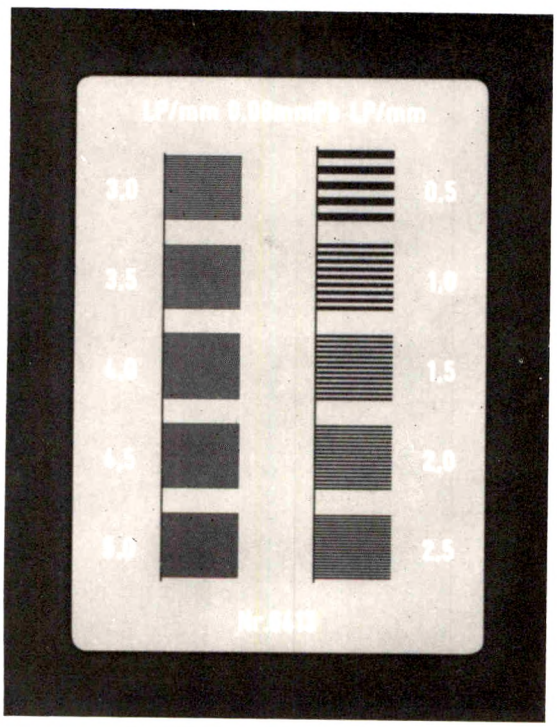


Fig. 2. Lead bar test object.

Several authors have pointed out that the illuminance distribution cannot be determined, in general, for a double-coated film by scanning the density pattern in both emulsion layers simultaneously, that is, treating the film as a whole.[2,4,7] However, if the illuminance distributions in the two emulsions are the same, then the film can be treated as a unit. Since the distributions in the screen-film systems examined in this paper are essentially the same, the film has been treated as a unit. From a series of roentgenograms of the lead bar test object having a considerable range of density levels, the SWRF was found to be independent of the level of exposure, as the definition given by Equation 1 requires, indicating that development effects were insignificant for the film-process system used. This means that widestep sensitometry can be used to relate densities to relative exposures in slit images, as well as in square wave images.

SWRF CALCULATED FROM LSF

Any image pattern on the film can be obtained by convoluting a one-dimensional input to the screen-film system with the LSF, when the conditions of linearity and spatial invariance (discussed in a previous paper[4]) are fulfilled. If these conditions are satisfied, it is a relatively simple matter to calculate the SWRF from the LSF by means of the convolution integral. We shall show that, for conventional screen-film systems, the SWRF can indeed be calculated from the LSF.

Let the object $O(\xi;\nu)$ be a one-dimensional square wave x-ray irradiance distribution absorbed in the screen-film system. The symbol ξ represents the spatial coordinate in the object. The fundamental spatial frequency ν enters as a parameter in $O(\xi;\nu)$ to indicate that the spatial square wave distribution depends on the fundamental spatial frequency. Furthermore, let $L(\xi)$ be the LSF of the screen-film system. Then, the illuminance distribution, $I(x)$, in the image can be found from the convolution integral

$$I(x;\nu) = \int_{-\infty}^{\infty} O(\xi;\nu)L(x-\xi)d\xi, \quad (2)$$

where x is the spatial coordinate in the one-dimensional image. Since we are interested in the deviation of $I(x;\nu)$ and $O(\xi;\nu)$ around their average values, we shall assume that $O(\xi;\nu)$ alternates between $+1$ and -1. (Since only relative values are important, the choice of $+1$ and -1 is made for convenience.) If we choose the origin of the coordinate system such that $O(\xi;\nu)$ becomes an even function and since $L(\xi)$ is also an even function, a maximum in the image pattern occurs when $x=0$. For $x=0$, we obtain

$$\begin{aligned} I(0;\nu) &= \int_{-\infty}^{\infty} O(\xi;\nu)L(-\xi)d\xi \\ &= 2\int_{0}^{\infty} O(\xi;\nu)L(\xi)d\xi. \end{aligned} \quad (3)$$

$I(0;\nu)$ represents the amplitude in the image of a lead bar pattern of fundamental spatial frequency ν.

The integration of the right-hand side of Equation 3 can be performed easily on a digital computer. For example, if the period of the square wave pattern is 400 microns (fundamental frequency of 2.5 cycles/mm.), Equation 3 becomes

$$I(0;\nu) = 2\left[\int_{0}^{100} L(\xi)d\xi - \int_{100}^{300} L(\xi)d\xi + \int_{300}^{500} L(\xi)d\xi \cdots\right]. \quad (4)$$

The SWRF is determined by the amplitudes $I(0;\nu)$ for various fundamental spatial frequencies ν.

By means of this approach the SWRF of Kodak Royal Blue Medical X-ray Film (ESTAR Base) exposed with 2 fast screens (barium lead sulfate) was calculated from the measured line spread-function. Care was taken to measure the LSF to low values at large distances, which is necessary for the evaluation of enough terms in Equation 4 to give sufficiently accurate results. Also the SWRF was measured directly from a roentgenographic exposure of the lead bar test object. Figure 3 shows good agreement of measured and calculated values. For comparison, the MTF of the same screen-film system is also given. A similar experiment with medium-speed screens (calcium tungstate) and Blue Brand Film also gave good agreement between the measured SWRF and that calculated from the LSF.

DEPENDENCE ON RADIATION QUALITY

In a previous paper[8] it was shown that the LSF is invariant with kilovoltage in the range of 50 to 110 kvp.* Since the LSF is invariant with radiation quality, this also should be the case for the SWRF. To confirm this, the following experiments were performed. Roentgenograms were made of the lead bar test object with a screen-film system consisting of medium-speed screens (calcium tungstate) and Blue Brand Film. The exposures were made with 70 kvp. radiation, filtered by 2 mm. Al, 0.5 mm. Cu plus 1 mm. Al, and 2.0 mm. Cu plus 1 mm. Al, resulting in half-value layers of 0.10,

* In this paper, the abbreviations kvp. and kvcp. have been used to denote the peak kilovoltage of a pulsating potential and kilovoltage, constant potential, respectively.

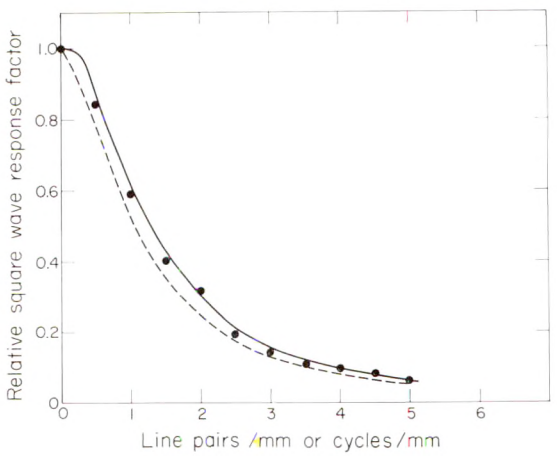


FIG. 3. Comparison of measured square wave response function (SWRF) (indicated by dots) and SWRF calculated from line spread-function (solid line) for Kodak Royal Blue Medical X-ray Film (ESTAR Base) exposed with 2 fast screens (barium lead sulfate). For comparison, the modulation transfer function of the same screen-film system is given by dashed curve.

0.25, and 0.45 mm. Cu, respectively. The SWRF was determined for these radiation qualities. As shown in Figure 4, the SWRF of the screen-film system is indeed independent of the radiation qualities used in this experiment. The same conclusion was reached for this range of radiation qualities when Blue Brand Film was exposed with a pair of fast screens (barium lead sulfate). These experiments tend to confirm previous results which showed that the LSF is constant over a limited range of radiation qualities.[8]

The use of high kilovoltages is becoming more common in medical roentgenography. Therefore, it is of interest to investigate the SWRF of screen-film systems under such conditions, since the scattering of x rays and the range of secondary electrons in the screens might introduce changes in the SWRF at high kilovoltages. For this purpose roentgenograms were made of the lead bar test object with 50, 125, and 200 kvcp. radiation, all filtered by 0.5 mm. Cu at the tube. The half-value layers for these radiation qualities were 0.18, 0.70, and 1.25 mm. Cu, respectively. The screen-film system consisted of a pair of fast screens (barium lead sulfate) and Blue Brand Film. As shown in Figure 5, the square wave response is constant in the 50–200 kilovoltage range. The same conclusion was reached for Blue Brand Film sandwiched between a pair of medium speed screens (calcium tungstate).

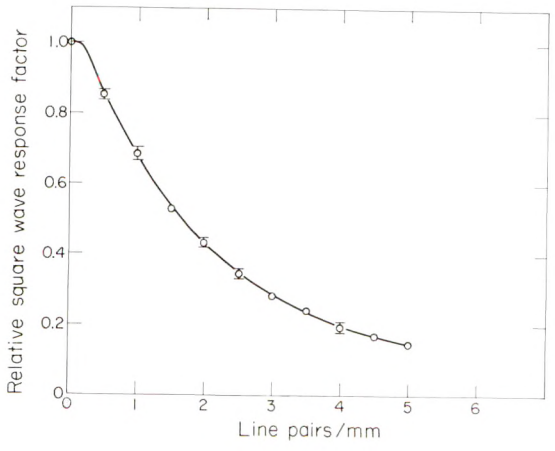


Fig. 4. Average square wave response function of Kodak Blue Brand Medical X-ray Film (ESTAR Base) and 2 medium-speed screens for 3 conditions of filtration. Exposures were made with 70 kvp. x rays filtered by 2 mm. Al, 0.5 mm. Cu plus 1 mm. Al, and 2 mm. Cu plus 1 mm. Al. The nonsystematic variation at certain line pairs/mm. is indicated.

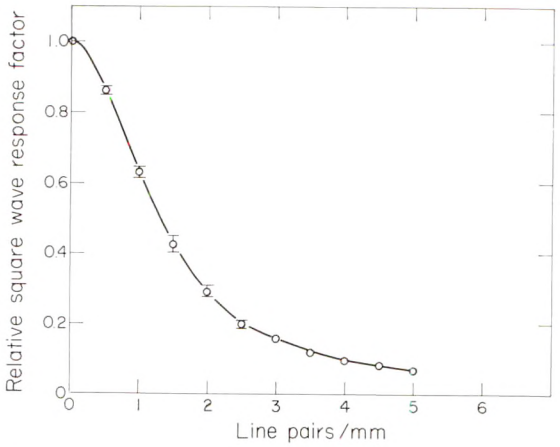


Fig. 5. Average square wave response function of Kodak Blue Brand Medical X-ray Film (ESTAR Base) and 2 fast screens exposed with 50, 125, and 200 kvcp. radiation, all filtered by 0.50 mm. Cu. The nonsystematic variation at certain line pairs/mm. is indicated.

Multiple Slit Scanning Technique

Square wave response function measurements presented in this paper indicate that it is desirable to use square wave test objects having spatial frequencies higher than 5 line pairs/mm. However, it is difficult to measure the SWRF accurately, particularly at high spatial frequencies. The uncertainty in the measurement at high frequencies arises from granularity of the film. The granularity causes noise in the microdensitometer traces and this gives rise to uncertainties in the SWRF for high spatial frequencies where the modulation is low. Of course, an average taken over many cycles increases the accuracy substantially. However, such an averaging procedure is time-consuming.

The averaging might be accomplished by scanning the square wave image with a number of parallel slits instead of only one slit. This procedure was described by Lam-

berts and co-workers[3] for MTF evaluation of photographic films. The possibility of using this technique for screen-film systems employing double-coated films seems worthy of investigation.

SUMMARY

The square wave response function (SWRF) is a convenient means for comparing the light-diffusion properties of screen-film systems; SWRF's are presented in this paper for several common screen-film systems.

Experiments have shown that the measured SWRF is in agreement with that calculated from the line spread-function.

The invariance of the SWRF with x-ray energy is demonstrated over a wide range of radiation qualities.

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Seventieth Annual Meeting: Washington-Hilton Hotel, Washington, D. C., September 30–October 3, 1969.

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Fifty-second Annual Meeting: Hotel Coronado, San Diego, Calif., March 1–6, 1970.

EDITORIAL

THE SEVENTIETH ANNUAL MEETING OF THE AMERICAN ROENTGEN RAY SOCIETY

THE eyes of the world are frequently turned on Washington, D. C., so that the people of the world may have a greater insight into current events and future developments. From September 30 through October 3, 1969, the eyes of the world of Radiology, for similar reasons, will also be turned on Washington, D. C. These dates encompass the official time of the Seventieth Annual Meeting of the American Roentgen Ray Society. The exact location is the Washington-Hilton Hotel, where unparalleled facilities exist for the needs of our Society.

The city itself is most attractive from the standpoint of beauty and its natural contours and waterways, as well as its historic and architectural significance. Washington is served by three major air ports. It has good railroad facilities and fine highway connections with ample parking space adjacent to the hotel.

Registration will begin at 2:00 P.M. on Sunday, in the Concourse connecting the Hilton International Ball Room and the Exhibit Hall and will be opened thereafter from 8:00 A.M. to 5:00 P.M.

On Monday, September 29, under the able direction of Dr. Ralph Caulk, Past President, the Annual Golf Tournament will be held at the Kenwood Golf and Country Club, where a luncheon will be available and dinner will be served. The tournament is open to all members and guests of the Society and free bus transportation will be provided to the Club and for the return trip. This is a beautiful course. Golf carts and caddies will be available. The Willis F. Manges Trophy will be awarded for the low net score, and the Exhibitor's Trophy for the low gross score. There also will be excellent tennis courts for those who favor tennis playing. Many other prizes will be awarded at the Golf and Tennis Dinner for the competing members and guests. Tickets will be available through Dr. Caulk or members of his Committee. Those who wish and who can arrange their own transportation may play in the morning, although the Golf Tournament does not begin until the afternoon. Dinner is planned for 7:15 P.M. and will be preceded by cocktails.

The Society is fortunate to again have Dr. Charles Bickham, Jr., serve as Chairman of the Committee on Local Arrangements. Mrs. Bickham, as Chairwoman of the Ladies' Committee, has prepared an outstanding program for our consorts, which will commence on Monday, September 29, with a tour covering the highlights of our Nation's Capital. This is a completely lectured, riding tour with stops to visit the Lincoln Memorial, and the Arlington National Cemetery, to see the changing of the guard at the Tomb of the Unknowns, and J. F. Kennedy's grave site. Other points of interest will be explained during the course of the trip, including the principal public and government buildings and shopping centers.

On Tuesday, September 30, there will be a guided tour of the new State Department's Diplomatic Reception Rooms, which contain magnificient furnishings and many exquisite paintings of historic interest. This will be followed by a visit to the famous Ford Theatre, which has recently been restored, and the Lincoln Museum. A luncheon at the Evans Farm Inn, located

in nearby McLean, Virginia, will be a featured attraction. Excellent food is promised.

On Wednesday, October 1, there is planned: "An Afternoon on Embassy Row." The "Afternoon" includes visits to 2 of the leading Embassies (not visited formerly), where cultural programs and entertainment will be presented. High ranking officials of each Embassy will extend a warm welcome and light refreshments will be served at the second Embassy of the visit.

On Thursday, October 2, the Ladies should be delighted by a visit to Woodlawn Plantation and Frank Lloyd Wright's Pope-Leighey House. A most enjoyable luncheon at Country Inn Dining on "Kings House Hill" at the Lazy Susan Inn in Woodbridge, Virginia, will be served on the return trip.

Tickets for all these tours can be purchased at the Ladies' desk in the Concourse. There will be a Ladies' Hospitality room in the Cabinet Room just off of the Concourse which will be open for complimentary coffee during the mornings of the meeting.

The Seventieth Annual Meeting will officially be called to order at 8:30 A.M. on Tuesday, September 30, by President Stephen W. Brown. Immediately thereafter President Brown assisted by Dr. Eugene Van Epps, Chairman of the Executive Council will install Dr. James C. Cook as the new President of the Society.

After a brief Inaugural Address the Scientific Sessions will begin. Forty-nine papers have been selected by the Program Committee for presentation. An innovation to this year's program has been added through the cooperation of the American Radium Society, The Society for Pediatric Radiology, and The Society of Neuroradiology. Each of these Societies has selected a paper, from those given at their 1969 meetings which was thought to be of most interest to all radiologists, and these papers are included in our program. Special awards will be given by the American Roentgen Ray Society to the authors of these presentations.

The complete program including titles and authors can be found elsewhere in this issue of the JOURNAL.

The First Scientific Session will follow the President's Inaugural Address, at approximately 8:55 A.M. on Tuesday and will finish promptly at 12:30 P.M. The Scientific Sessions on Wednesday through Friday will begin at 8:30 A.M. and finish likewise promptly at 12:30 P.M.

The Technical Exhibits will be open each day from 8:30 A.M. to 6:00 P.M., except on Friday when they will close at 1:30 P.M. This integral part of the meeting has been most competently arranged by Dr. E. F. Lang, Manager of the Annual Meeting, expertly advised and ably assisted by Mr. Clifford L. Sherratt, Honorary Member of the Society. No formal function is planned between 12:30 P.M. and 3:00 P.M., so that members and guests will have time to visit the booths housing the displays of our distinguished Technical Associates.

Dr. William A. Hanafee, assisted by other members of his Committee, has assembled excellent and most instructive Scientific Exhibits which will be displayed in the Exhibit Hall of the Washington-Hilton Hotel.

On Tuesday evening, September 30, the Caldwell Lecture will be delivered by J. Scott Dunbar, M.D., F.R.C.P.(C), Professor and Chairman of the Department of Diagnostic Radiology, McGill University, and Director of the Department of Radiology, Montreal Children's Hospital, Montreal, P.Q., Canada. He has chosen as his subject "Upper Respiratory Tract Obstruction in Infants and Children." Dr. Dunbar will be introduced by Dr. Robert G. Fraser, Radiologist-in-Chief of the Department of Diagnostic Radiology, Royal Victoria Hospital, Montreal, P. Q., Canada, who is his long-time friend and Associate.

Instruction Courses will be presented on Tuesday, Wednesday and Thursday from 8:30 A.M. to 5:00 P.M. and on Friday from

1:30 P.M. to 3:00 P.M. Dr. Harold O. Peterson, the Director has, as usual, obtained an outstanding Faculty. Abstracts of these Courses with information for registration will be published in the August issue of this JOURNAL. Members and guests are advised to register early to be assured of being able to attend the Course of their choice.

A Cocktail Party in the International Ball Room, East, at 6:30 P.M. on Thursday, October 2, will precede the Annual Banquet. There will be music for cocktails, dinner and dancing. At this time, the awards for the outstanding scientific exhibits will be presented and there will be no speeches. Tickets will be on sale Tuesday, Wednesday and Thursday at the registration desk in the Concourse. In addition to the fine music, an outstanding floor show has been arranged by Dr. Bickham and his Committee.

All radiologists, interested physicians, members and guests are cordially invited to attend this Seventieth Annual Meeting of the American Roentgen Ray Society.

JAMES C. COOK, M.D.
President-Elect

LL 14 Professional Plaza
Detroit, Michigan 48201

PRELIMINARY PROGRAM

SEVENTIETH ANNUAL MEETING OF THE AMERICAN ROENTGEN RAY SOCIETY

The Seventieth Annual Meeting of the American Roentgen Ray Society will be held at the Washington-Hilton Hotel, Washington, D.C., Tuesday through Friday, September 30 to October 3, 1969.

The Executive Council will meet Sunday, September 28, 9:00 A.M. in the Georgetown Room W.

On Monday, September 29, the Annual Golf and Tennis Tournaments will be held at the Kenwood Golf and Country Club. Guests as well as members are invited to participate. Competition will be for the Willis F. Manges and the Exhibitor's Trophies, and other awards. At 7:15 P.M. the same evening the Annual Golf and Tennis Dinner will begin, an event always enjoyed by golfers and non-golfers alike. Transportation from the hotel to the Club and return will be provided.

Scientific Sessions will be held each morning, Tuesday through Friday, beginning at 8:30 A.M. and continuing to 12:30 P.M., in the Hilton International Ball Room. Dr. J. Scott Dunbar, Professor and Chairman of the Department of Diagnostic Radiology, McGill University, and Director of the Department of Radiology, Montreal Children's Hospital, Montreal, P. Q., Canada, will deliver the Caldwell Lecture on Tuesday evening at 8:30 P.M. in the Hilton International Ball Room.

Instruction Courses will be offered from 3:00 P.M. to 4:30 P.M. on Tuesday, Wednesday and Thursday and from 1:30 P.M. to 3:00 P.M. on Friday. The detailed plan of the Instruction Courses will be published in the August issue of the JOURNAL.

Scientific Exhibits will be on display in the Exhibit Hall from 8:30 A.M. each morning Monday through Friday. These Exhibits will close at 8:00 P.M. on Tuesday, 9:00 P.M. on Wednesday, 7:30 P.M. on Thursday and 1:30 P.M. on Friday.

Technical Exhibits will be located in the Exhibit Hall also. They will open each morning at 8:30 A.M. and will close at 6:00 P.M., Tuesday through Thursday and at 1:30 P.M. Friday.

The Annual Banquet will be held Thursday evening at 7:30 P.M. in the Hilton International Ball Room, preceded by cocktails served in the East portion of the Ball Room beginning at 6:30 P.M.

The Program Committee, under the Chairmanship of President-Elect James C. Cook, has arranged the following program for the Scientific Sessions.

Tuesday, September 30, 1969
Hilton International Ball Room

8:30 A.M.

Call to Order, Seventieth Annual Meeting: Stephen W. Brown, M.D., Augusta, Georgia, President.

Installation of President-Elect, James C. Cook, M.D., Detroit, Michigan, by Stephen W. Brown, M.D., Augusta, Georgia, President, and Eugene Van Epps, M.D., Durham, North Carolina, Chairman of the Executive Council.

Presentation of Past Presidents' Book to Stephen W. Brown, M.D., by James C. Cook, M.D.

Presidential Address: President James C. Cook, M.D.

8:55 A.M.

Presiding: James C. Cook, M.D.
Detroit, Michigan

1. *Award Paper, Society for Pediatric Radiology.* This paper will be chosen by the Society for Pediatric Radiology at their Twelfth Annual Meeting, September 28–29, 1969. It will be the presentation considered to be of greatest interest to all radiologists.
2. Transient Respiratory Distress of the Newborn; A Temporary Disturbance of a Nor-

mal Phenomenon. Leonard E. Swischuk, M.D. (by invitation), Oklahoma City, Okla.

3. Excretion of Urographic Contrast Media (Meglumine Diatrizoate) in the First Month of Life; An Experimental Study. M. B. Nogrady, M.D. (by invitation), Montreal, P. Q., Canada, N. Khan, M.D. (by invitation), Montreal, P. Q., Canada, W. J. Alexander, M.D. (by invitation), Montreal, P. Q., Canada, K. Drummond, M.D. (by invitation), Montreal, P. Q., Canada, and H. Whittaker, M.Sc. (by invitation), Montreal, P. Q., Canada.
4. Urinary Tract Pathology with Sepsis. Chas. E. Shopfner, M.D., Kansas City, Mo.
5. Giant Hydronephrosis in Infants and Children; Value of High Dosage Excretory Urography in Predicting Renal Salvage Ability. Walter E. Berdon, New York, N. Y., David H. Baker, New York, N. Y., Selwyn Levitt (by invitation), New York, N. Y., Joshua Becker (by invitation), New York, N. Y., and Aurelio Uson (by invitation), New York, N. Y.
6. Cystography in Childhood: Tumors and Pseudotumors. Arthur S. Tucker, Cleveland, Ohio, and Lester Persky (by invitation), Cleveland, Ohio.
7. Irradiation of the Pituitary and Base of Skull in Histiocytosis X. Alan E. Oestreich, M.D. (by invitation), Rochester, N. Y., Philip Rubin, M.D. (by invitation), Rochester, N. Y., and Lionel W. Young, M.D. (by invitation), Rochester, N. Y.
8. The Nevoid Basal Cell Carcinoma Syndrome. Gerald D. Dodd, M.D., Houston, Tex., Bao-Shan Jing, M.D., Houston, Tex., and David E. Anderson, Ph.D. (by invitation), Houston, Tex.
9. Simultaneous Frontal and Lateral Chest Roentgenograms of Low Birth Weight Infants. Herman Grossman, M.D. (by invitation), New York, N. Y., Patricia Winchester, M.D. (by invitation), New York, N. Y., David Klain, M.D. (by invitation), New York, N. Y., and Peter A. Auld, M.D. (by invitation), New York, N. Y.
10. Renal Pseudotumors. Filemon A. Lopez, M.D. (by invitation), New York, N. Y.
11. Rapid Intra-Renal Circulation. Joshua A. Becker, M.D. (by invitation), New York, N. Y., Ira E. Kanter, M.D. (by invitation), New York, N. Y., and Stanley Perl, M.D. (by invitation), New York, N. Y.

Tuesday Evening, September 30, 1969
Eight-thirty O'Clock
Hilton International Ball Room

THE CALDWELL LECTURE

Upper Respiratory Tract Obstruction in Infants and Children

By

J. Scott Dunbar, M.D., F.R.C.P.(C)

Professor and Chairman of the Department of Diagnostic Radiology, McGill University, Montreal, P.Q., Canada; and Director of the Department of Radiology, Montreal Children's Hospital, Montreal, P.Q., Canada

Introduction by Robert G. Fraser, M.D., Radiologist-in-chief of the Department of Diagnostic Radiology, Royal Victoria Hospital, Montreal, P.Q., Canada; and Professor of the Department of Diagnostic Radiology, McGill University, Montreal, P.Q., Canada

Presentation of the Caldwell Medal to Doctor Dunbar by President Cook.

Wednesday, October 1, 1969
Hilton International Ball Room

8:30 A.M.

Presiding: Seymour F. Ochsner, M.D.
New Orleans, Louisiana

12. Radiological Findings in Occupational Acro-osteolysis. Walter M. Whitehouse, M.D., Ann Arbor, Mich., Theodore Ditchek, M.D. (by invitation), Phoenix, Ariz., Bertram D. Dinman, M.D. (by invitation), Ann Arbor, Mich., Vernon N. Dodson, M.D. (by invitation), Ann Arbor, Mich., and Harold J. Magnuson, M.D. (by invitation), Ann Arbor, Mich.
13. *Award Paper, American Radium Society.* Chemotherapy of Malignant Tumors, C. G. Zubrod, M.D., Scientific Director for the Department of Chemotherapy, National Cancer Institute, Bethesda, Maryland. This paper, which was considered to be of greatest interest to all radiologists, was chosen at the Fifty-first Annual Meeting of the American Radium Society.
14. Breast Cancers Found on Repetitive Examination in Mass Screening. Philip Strax, New York, N. Y., Louis Venet (by invitation), New York, N. Y., and Sam Shapiro (by invitation), New York, N. Y.
15. Xeroradiography. John N. Wolfe, M.D. (by invitation), Detroit, Mich.

16. Evaluation of Metastatic Carcinoma of the Prostate by Serial Bone Scanning. Donald P. Harrington, M.D. (by invitation), Minneapolis, Minn., John M. Wolff, M.D. (by invitation), Minneapolis, Minn., and Merle K. Loken, M.D., Minneapolis, Minn.
17. Time Sequence Tomography in Arteriography of the Pancreas. H. Herlinger (by invitation), Leeds, England.
18. Tomoscopy and Related Matters. W. E. Crysler, M.D., Brantford, Ont., Canada.
19. Television Image Processing Techniques for Radiological Diagnosis. Harold L. Kundel, M.D. (by invitation), Philadelphia, Pa., Herbert M. Stauffer, M.D., Philadelphia, Pa., and Charles M. Haas (by invitation), Philadelphia, Pa.
20. Tomography of the Mastoids in the Basal Projection. William N. Hanafee, M.D., Los Angeles, Calif., Ruth Gussen, M.D. (by invitation), Los Angeles, Calif., and Robert W. Rand, M.D. (by invitation), Los Angeles, Calif.
21. Visualization of the Retropharyngeal and Retro-esophageal Space on Plain Film: An Aid in Evaluating the Prevertebral Soft Tissues. Joseph P. Whalen, M.D. (by invitation), New York, N. Y., and C. Lawrence Woodruff, M.D. (by invitation), New York, N. Y.
22. Laryngography of Benign Lesions; The Evaluation Procedure of Choice. Thomas H. Johnson, Jr., M.D., Pittsburgh, Pa., and John H. Feist, M.D., Pittsburgh, Pa.
23. Leg Edema Resulting From Caval Thrombosis. Klaus Ranniger, M.D. (by invitation), Chicago, Ill.
24. Beam Quality Measurements in Diagnostic Roentgenology. II. E. Dale Trout, B.S., Corvallis, Ore., John P. Kelley, B. S. (by invitation), Corvallis, Ore., and Kenneth E. Weaver, M.S. (by invitation), Corvallis, Ore.

Thursday, October 2, 1969
Hilton International Ball Room

8:30 A.M.

Presiding: Eugene Van Epps, M.D.
Durham, North Carolina

25. Lipomas of the Spinal Canal. Lawrence H. A. Gold (by invitation), Minneapolis, Minn.
26. *Award Paper, American Society of Neuroradiology*. Radiographic Anatomy of the Posterior Cerebral Artery and Its Variations. M. T. Margolis, Department of Radiology, San Francisco Medical Center, School of Medicine, San Francisco, California, and T. H. Newton, Department of Radiology, San Francisco Medical Center, School of Medicine, San Francisco, California. This paper, which was considered to be of greatest interest to all radiologists, was chosen at the Seventh Annual Meeting of the American Society of Neuroradiology.
27. Epidermoid and Dermoid Cysts. Bert Lincoln Pear, M.D., Denver, Colo.
28. Arteriographic Evaluation of Carotid Artery Surgery. Frank E. Maddison (by invitation), Milwaukee, Wis.
29. Thickening of the Skull in Surgically Treated Hydrocephalus. R. E. Anderson (by invitation), Minneapolis, Minn., S. A. Kieffer (by invitation), Minneapolis, Minn., J. Wolfson (by invitation), Minneapolis, Minn., H. O. Peterson, Minneapolis, Minn., and D. Long (by invitation), Minneapolis, Minn.
30. Glioblastoma Multiforme: An Analysis of the Results of Postoperative Radiotherapy Alone *vs.* Radiotherapy and Concomitant 5-Fluorouracil; A Prospective Randomized Study of 32 Cases. Robert W. Edland, M.D., Madison, Wis., Manucher Javid, M.D. (by invitation), Madison, Wis., and Fred J. Ansfield, M.D. (by invitation), Madison, Wis.
31. The Atrial Septal Sign; A Key Indicator in the Interpretation of Angiocardiograms. Kent Ellis, M.D. (by invitation), New York, N. Y., Ira E. Kanter, M.D. (by invitation), New York, N. Y., Donald L. King, M.D. (by invitation), New York, N. Y., and John O. Burris, M.D. (by invitation), New York, N.Y.
32. Bone Changes after Dilantin Treatment. Kenneth R. Kattan (by invitation), Cincinnati, Ohio.
33. Peritubular Adhesions. George Stassa, M.D. (by invitation), New York, N. Y., and Ina R. Altman, M.D. (by invitation), New York, N. Y.
34. Cineradiographic Studies in Tricuspid Stenosis. Charles F. Wooley, M.D. (by invitation), Columbus, Ohio, and William Molnar, M.D., Columbus, Ohio.
35. Angiography in the Evaluation of Patients for Abdominal Aortic Surgery. Paul C. Khan, M.D. (by invitation), Boston,

Mass., Warren C. Widrich, M.D. (by invitation), Boston, Mass., John M. Moran, M.D. (by invitation), Boston, Mass., and Allan D. Callow, M.D. (by invitation), Boston, Mass.

36. Usefulness of Serial Magnification Technique in Angiography. Constantin Cope, M.D. (by invitation), Philadelphia, Pa., and Harold J. Isard, M.D., Philadelphia, Pa.
37. Radiographic Evaluation of Cardiac Transplantation. Edward B. Singleton, M.D., Houston, Tex., Joseph Colquhoun, M.D. (by invitation), Houston, Tex., Louis L. Leatherman, M.D. (by invitation), Houston, Tex., John D. Milam, M.D. (by invitation), Houston, Tex., Denton A. Cooley, M.D. (by invitation), Houston, Tex., and Thomas S. Harle, M.D. (by invitation), Houston, Tex.

Friday, October 3, 1969
Hilton International Ball Room

8:30 A.M.

Presiding: Herbert M. Stauffer, M.D.
Philadelphia, Pennsylvania

38. Small Airways Disease: A Clinical Roentgenologic Pathologic Correlation. Peter T. Macklem, M.D. (by invitation), Montreal, P.Q., Canada, W. M. Thurlbeck, M.D. (by invitation), Montreal P.Q., Canada, and Robert G. Fraser, M.D., Montreal P.Q., Canada.
39. Pulmonary Aspergillosis. Wallace T. Miller, M.D., Philadelphia, Pa., and Robert A. Zimmerman, M.D. (by invitation), Philadelphia, Pa.
40. A Guided Brush for Bronchial Brush Biopsy. James K. V. Willson, M.D., Mobile, Ala., Marshall Eskridge, M.D. (by invitation), Mobile, Ala., and William J. Bean, M.D. (by invitation), New Orleans, La.
41. Radiation Effect on the Bronchial Tree. S. F. Boushy (by invitation), Houston, Tex., A. H. Helgason (by invitation), Houston, Tex., and Luceil B. North, Houston, Tex.
42. Sputum Cytopathology and Roentgen Correlation of Pulmonary Oil Embolization Following Lymphangiography. Mark D. Reiss, M.D. (by invitation), Baltimore, Md., and M. Wilson Toll, M.D. (by invitation), Baltimore, Md.
43. Abdominal Lymph Node Scintiscanning for Diagnosis and Treatment of Lymphoma. Alexander W. Pearlman (by invitation), New York, N. Y.
44. Unravelling the Tangled Sigmoid—A New Approach to Routine Angulation of the Tube. Theodore Perl, M.D., Syracuse, N. Y., and William Goldman, M.D. (by invitation), Syracuse, N. Y.
45. Comparative Evaluation of the Sequential Use of Radiation and Surgery in Primary Tumors of the Oral Cavity, Oropharynx, Larynx and Hypopharynx. Quintous E. Crews (by invitation), San Diego, Calif., and Gilbert H. Fletcher, Houston, Tex.
46. The Gastric Camera—A Method for *In Vivo* Radiologic-Pathologic Correlation. Barbara M. Kadell, M.D. (by invitation), Los Angeles, Calif., Marvin Weiner, M.D. (by invitation), Los Angeles, Calif., John N. Johnson, M.D. (by invitation), Los Angeles, Calif., and Martin A. Pops, M.D. (by invitation), Los Angeles, Calif.
47. Prolapsed Gastric Mucosa Through a Gastro-jejunostomy. William B. Seaman, New York, N. Y.
48. The Significance of Residual Collections of Opaque Media in Gastrointestinal Disease. Sidney W. Nelson, M.D., Columbus, Ohio.
49. Granulomatous Colitis in Association with Diverticula. Richard H. Marshak, New York, N. Y., Bernard S. Wolf, New York, N. Y., Daniel Present (by invitation), New York, N. Y., and Monsho Khilnani (by invitation), New York, N. Y.

INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION (ICRP)

The Commission and its Committees met in Oxford, England, in April, 1969, to review work being carried out by Committees and Task Groups, and to plan the ICRP's program of work during the coming years. Work on a number of topics is near to completion in the Task Groups that have been set up to study specific problems, and it is expected that reports on many of the following subjects will be ready for publication within the next year:

Protection of the patient in radionuclide investigations
Protection of the patient in radiodiagnostic procedures
Protection against external radiations (a comprehensive revision of ICRP Publications 3 and 4)
Radiation protection in educational establishments
Radiation dose from neutrons and protons in the energy range from 400 MeV to 2 GeV.
Biological effects of inhaled radioactive particulates
Anatomical, physiological and metabolic characteristics for the "Reference Man"
Metabolism of plutonium and related elements, and their compounds
Protection against radon, thoron and their daughter products
Local retention functions of bone-seeking radionuclides
A comprehensive review of ICRP Publication 2
The assessment of internal contamination resulting from recurrent or prolonged intakes of radionuclides.

At the Oxford meeting Task Groups were established to report on a number of subjects of importance to the Commission's field of work, including the relative biological effectiveness of neutrons with respect to mutagenesis; the balance between genetic effects in the first generation *versus* later generations; the feasibility of epidemiological surveys of human populations for improving knowledge of radiosensitivity and dose-response relationships; respiratory absorption and elimination mechanisms; and principles and general procedures for handling emergency and accidental exposures of workers.

The Commission decided to issue the following amendments to its recommendations that appeared in ICRP Publication 9:

Dose limit to the lens of the eye. In its most recent recommendations (ICRP Publication 9, paragraph 25) the Commission included the lenses of the eyes amongst the most radiosensitive tissues when exposed to radiations of high LET. The Commission therefore recommended the use of a special Modifying Factor for irradiation of the lenses of the eyes (paragraph 16).

A recent review by an ICRP Task Group to consider the relative radiosensitivities of different tissues (ICRP Publication 14) concluded: "The human evidence suggests that the annual dose limit for exposure of the lens of the eye should be 15 rems for both low and high LET radiation. There is no need for the additional modifying factor used at present when QF>1."

The Commission endorses this conclusion of the Task Group and recommends that the dose limit for the lens of the eye be 15 rems, without the use of an additional modifying factor.

Quality Factor for β^-, β^+ and e^- radiations with maximum energy ≤ 0.03 MeV. In ICRP Publication 9, paragraph 17, the Commission recommended a value of 1.7 as being the appropriate Quality Factor for β^-, β^+ and e^- radiations with maximum energy ≤ 0.03 MeV. The Commission has reviewed the biological and physical evidence related to this point, and concludes that a value of unity is appropriate within the degree of precision required for the purposes of radiological protection. The Commission therefore recommends that QF be taken as 1 for all β^-, β^+, e^-, γ and X-radiations, and for conversion electrons. F. D. Sowby, Scientific Secretary, ICRP.

NEWS ITEMS

DIAGNOSTIC RADIOLOGY OF THE URINARY TRACT

Department of Radiology, University of Minnesota

This Course is designed primarily for radiologists and urologists. It will cover in detail the radiologic evaluation of the entire urinary system, stressing newer knowledge and procedures.

The Course will be held October 27–31, 1969, in the Mayo Memorial Auditorium of the University of Minnesota Health Sciences Center, Minneapolis.

The Course Content is as follows: Anatomy, embryology, physiology, and pathology of the urinary tract; investigative procedures (urography, nephrotomography, renal angiography, and cyst puncture); radioisotope studies of renal function and anatomy; contrast media and reactions; congenital abnormalities of the urinary tract; voiding cystourethrography, its present status; evaluation of renovascular hypertension; inflammatory disease of the urinary tract; evaluation of the renal mass lesion; trauma to the urinary tract and its sequelae; lesions of the adrenal glands; and evaluation of renal transplants.

An outstanding Faculty has been assembled for the Course. These include: Dr. Joshua A. Becker, New York, New York; Dr. Eric Boijsen, Lund, Sweden; Dr. John L. Emmett, Rochester, Minnesota; Dr. Richard M. Friedenberg, Bronx, New York; Dr. Glen W. Hartman, Rochester, Minnesota; Dr. Sadek Hilal, New York, New York; Dr. Anthony F. Lalli, Ann Arbor, Michigan; Dr. Harry Z. Mellins, Brooklyn, New York; Dr. John S. Najarian, University of Minnesota Medical School; Dr. A. J. B. Palubinskas, San Francisco, California; Dr. Charles E. Shopfner, Kansas City, Missouri; Dr. John R. Thornbury, Ann Arbor, Michigan; Dr. Ross M. Tucker, Rochester, Minnesota; and Dr. David M. Witten, Rochester, Minnesota.

This Continuation Course will be presented under the direction of Dr. Harold O. Peterson, Professor and Head, Department of Radiology, and Dr. Eugene Gedgaudas, Associate Professor and Director, Division of Diagnostic Radiology, University of Minnesota Medical School. The remainder of the Faculty will include members of the teaching staff of the University of Minnesota Medical School.

The Annual Leo Rigler Lecture will be given on Wednesday evening, October 29, 1969 by Dr. Eric Boijsen.

A series of social events has been planned for participants and their wives.

For further information, please write to: Director, Continuation Medical Education, Nolte Center for Continuing Education, University of Minnesota, Minneapolis, Minnesota 55455.

NUCLEAR MEDICINE: DIAGNOSIS AND TREATMENT OF DISEASE WITH RADIONUCLIDES GIVEN INTERNALLY

American College of Physicians

A Course on the above subject will be given at the University of Michigan Medical Center, Ann Arbor, Michigan, under the Chairmanship of William H. Beierwaltes, M.D., F.A.C.P., November 3–7, 1969.

Lectures and demonstrations will be presented on the diagnosis and treatment of disease, utilizing internally administered radionuclides and radionuclide-labeled compounds (exclusive of sealed sources). Concepts will be stressed, with presently available applications cited as specific examples. All methods used in the University of Michigan Nuclear Medicine Clinical Unit will be passed out in printed form and will be illustrated by daily demonstrations. Recent and significant advances will be included.

The following subjects will be discussed by Guest Experts as well as the Faculty of the University of Michigan: radiation

biology and dosimetry; radionuclides and radiolabeled compounds; radiation detection instrumentation; the treatment of thyroid disease; and the diagnosis of diseases of the brain, parathyroid glands, lungs, liver, spleen, kidneys, bones, and malignant melanomas.

Requests for information and applications should be directed to Edward C. Rosenow, Jr., M.D. F.A.C.P., Executive Director, American College of Physicians, 4200 Pine Street, Philadelphia, Pa. 19104.

FIFTH ANNUAL SAN FRANCISCO CANCER SYMPOSIUM

The subject of this Symposium is: "Preoperative and Postoperative Radiation Therapy in the Treatment of Cancer."

It will be presented by the Zellerbach Saroni Tumor Institute and the Department of Surgery, Mount Zion Hospital and Medical Center, and will be held in the California Room of the St. Francis Hotel, Union Square, San Francisco, October 17 and 18, 1969 from 8:30 A.M. to 4:00 P.M.

Advance registration is required. The registration deadline is October 10, 1969.

For further information please contact: Jerome M. Vaeth, M.D., Director, Zellerbach Saroni Tumor Institute, 1600 Divisadero Street, San Francisco, Calif. 94115.

FELLOWSHIP IN RADIOLOGIC SCIENCE AND NUCLEAR MEDICINE

The Donner Laboratory, University of California, announces an opportunity for advanced study and research in radiologic science and nuclear medicine. Activities include investigation of the biologic effects of high-energy heavy particles, fast neutrons and pi mesons, participation in the use of high-energy particles in therapy, and the diagnostic, therapeutic and investigative uses of radioisotopes.

One or two courses in the graduate program in biophysics and medical physics may be taken concurrently.

Applicants should have had residency training in radiology, medicine, surgery, pediatrics etc. Stipend will be made available from a training grant, or the Laboratory will sponsor the individual's application for a direct fellowship.

Application forms are available from: John H. Lawrence, M.D., Director, Donner Laboratory, University of California, Berkeley, California 94720.

MODERN CONCEPTS OF RADIOLOGIC SPECIAL PROCEDURE TECHNIQUES AND ROOM DESIGN

A Course on this topic will be given September 4–6, 1969 at the Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, Missouri.

This Course will offer up-to-date information on room design and the selection of x-ray and accessory equipment necessary to perform modern radiologic special procedures.

The Faculty will include among others, Kurt Amplatz, M.D., John Campbell, M.D., David O. Davis, M.D., Harry Fischer, M.D., William Hanafee, M.D., P. Ruben Koehler, M.D., Stewart Reuter, M.D., Nikolaus Schad, M.D., Juan M. Taveras, M.D., and Michel Ter-Pogossian, Ph.D.

For further information please write to P. Ruben Koehler, M.D., Mallinckrodt Institute of Radiology, Washington University School of Medicine, 510 S. Kingshighway, St. Louis, Missouri 63110.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

ESSAI DE CLASSIFICATION DES DYSPLASIES SPONDYLOÉPIPHYSAIRES. By P. Maroteaux, Clinique de Génétique médicale, Hôpital des Enfants malades, Paris; R. Wiedemann and J. Spranger, Kinderklinik der Christian-Albrechts-Universität, Kiel; K. Koslowski, Clinique pédiatrique, Service de Radiologie, Cracovie; and L. Lenzi, Clinica Ortopedica dell'Università, Pavia. Paper. Pp. 93, with some illustrations. Publisher: Simep Editions, Lyon, France, 1968.

The authors propose a classification of certain skeletal dysplasias which have in common involvement of vertebrae, the round bones of the wrist and ankle, the epiphyses of the long bones and, at times, the adjacent metaphyses. As a group, these osseous affections are referred to as "spondylo-epiphyseal dysplasias." Clinically, they present with variable disturbances of articular function, disorders of gait, and diminution of stature. The pattern of involvement is variable: in some conditions, the trunk is disproportionately short; in others, there is micromelia of a degree which simulates achondroplasia. An outstanding feature in their evaluation is the relatively late clinical recognition. Most affected individuals are considered normal until the second year of life or even later in spite of subsequent severe dwarfism.

Among conditions arbitrarily excluded from consideration, notwithstanding vertebral, epiphyseal and even metaphyseal lesions, are Conradi's disease (dysplasia epiphysealis punctata), diastrophic dwarfism, metatropic dwarfism, and the mucopolysaccharidoses. These are excluded because their diagnostic features and evolution are considered to be clearly defined and different from the group under consideration.

The conditions considered are divided into 3 major groups, based on predominant involvement of the epiphyses, vertebrae, or of a combination of epiphyses and metaphyses.

The first major group, designated poly (multiple) epiphyseal dysplasias includes: (a) a subgroup with elective involvement of the epiphyses of the long bones and little or no spinal involvement; (b) a subgroup with involvement of the spine and proximal epiphyses but with normal hands and feet; and (c) a subgroup with localized epiphyseal involvement.

The second major group includes: (a) predominant spinal and minor epiphyseal involvement, the latter often restricted to the hips; (b) spinal involvement with severe involvement of the proximal epiphyses and occasional distal epiphyseal change; and (c) generalized vertebral and epiphyseal involvement.

The third major group includes: (a) epiphyseal and metaphyseal changes with little or no spinal involvement; (b) epiphyseal and metaphyseal changes with distinct spinal involvement; and (c) the pseudo-achondroplastic form of epiphyseal, metaphyseal and spinal involvement.

Each of the subgroups is described in detail, the descriptions purporting to provide a definition. The authors introduce a new term of Greek derivation, brachyomy (short trunk) for the first subgroup of the second major grouping. The complete classification is shown in Table 1 taken from their publication.

The authors freely admit that many entities have been overlooked and it is clear that others have been "forced to fit" their schema. Some, they state, cannot be classified with any precision. For the future study of these entities, they suggest that an international nomenclature be developed, but leave unspoken the thought that theirs might be a jumping-off point.

Unless an International Classification can be developed, the one suggested in this publication will be of confusional value to the practicing radiologist who has only occasional contact with dysplasias. The terminology is imprecise and the criteria for separation of one entity from another can be confusing. For the institutional radiologist who has more opportunity to collect examples of skeletal dysplasias, the criteria for separation are particularly difficult. How sharply defined are features described as "more or less localized," "almost isolated involvement," "severe involvement," etc.? These imply a quantitative judgement in an area where even qualitative evaluations lack distinct features.

Table I

Poly (Multiple) Epiphyseal Dysplasias	With elective involvement of the epiphyses of the long bones and of the extremities	Multiple epiphyseal dysplasia (Fairbank)
	With involvement of the spine and proximal epiphyses	
	More or less localized	Hip dysplasia Thiemann's disease Dysplasia of the elbows
Platyspondyly	With almost isolated spinal involvement	Brachyomy Spondylo-epiphyseal dysplasia tarda
	With severe involvement of the hips	Congenital spondylo-epiphyseal dysplasia
	With generalized epiphyseo-metaphyseal involvement	Morquio's disease Syndromes simulating Morquio's disease Spondylo-metaphyseal dysostosis
Epiphyseo-metaphyseal Dysplasias	Without spinal involvement	Generalized form Peripheral form of Silfverskiold (Pleonosteose of Leri)
	With spinal involvement	Complex dysplasias Pseudo-achondroplastic form

A more basic objection might be raised to this attempt at classification, and it applies equally to most others which we are obliged to use at the present stage of our knowledge. The fact that developmental skeletal lesions occur in certain patterns does not necessarily mean that all individuals with a given pattern of involvement have the same condition or that the same pattern is present in the infant, child and adult. We all operate on the assumption that a certain degree of similarity in pattern does have diagnostic meaning, but we part company when overlaps between one pattern and another occur. And the point at which we part company depends on how much of a "divider" or a "lumper" each of us happens to be. Consequently, to categorize entities on the basis of variable involvement of spine and epiphyses tends to imply relationships where none may exist. I hasten to point out that this implication is nowhere suggested by the authors, but it would help to have a disclaimer voiced. One might as well classify entities on the basis of predominant asymmetric involvement. We would then have to include hemihypertrophy, polyostotic fibrous dysplasia, Ollier's disease, melorrheostosis, and Trevor's disease (dysplasia epiphysealis hemimelica) among others as possibly related conditions. The classification would serve a purpose, as does the one by Maroteaux and his associates, of providing a list of conditions for consideration when a particular pattern of growth disturbances is recognized. But, for avoiding errors of classification and simplifying the work of researchers, something more fundamental is required.

Meanwhile, however, the serious considerations which have been given to this classification of spondylo-epiphyseal dysplasias, and the illustrations and descriptions of the various entities in this short monograph justify its place in all medical libraries, and especially in those used by students of normal and disturbed bone growth. Human geneticists will find the ma-

terial useful, but they will still require assistance from experienced radiologists to properly categorize dysplasias with spine and epiphyseal involvement.

If a functional international nomenclature for these and other entities can be developed, we shall owe the authors a great debt. This interesting, informative and provocative attempt at classification clearly indicates the need for a common terminology.

FREDERIC N. SILVERMAN, M.D.

ANGIOGRAPHY OF CEREBRAL CIRCULATION. By Kurt Decker and Herbert Backmund, Munich. Cloth. Pp. 76, with 148 illustrations. Price, $12.00. Georg Thieme Verlag, Stuttgart. In the USA and Canada, Intercontinental Medical Book Corporation, New York, N. Y. 10016, 1969.

This monograph is well written for the student and physician who wish to know the basic approach to reading cerebral angiograms.

The illustrations were selected from an extensive clinical experience with cerebral pathologies. The newer techniques of photographic subtraction, electronic subtraction and addition often yield clear-cut assurances of localized pathology. Color television photography projects a new dimension of contrast between areas of compression and hematoma.

The book is recommended for the skilled and non-skilled workers with neuroroentgenologic interests.

JAN NYBOER, D.Sc., M.D.

BOOKS RECEIVED

SURGERY OF THE CHEST. Second edition. Edited by John H. Gibbon, Jr., M.D., Formerly Samuel D. Gross Professor of Surgery, and Chairman of the Department of Surgery, The Jefferson Medical College, Philadelphia, Pa.; David C. Sabiston, Jr., M.D., Professor and Chairman, Department of Surgery, Duke University School of Medicine, Durham, N. C.; and Frank C. Spencer, M.D., George David Stewart Professor of Surgery and Chairman, Department of Surgery, New York University School of Medicine, New York, N. Y. Cloth. Pp. 954, with 621 illustrations. Price, $32.50, U.S., and $35.10 in Canada. W. B. Saunders Company, West Washington Square, Philadelphia, Pa. 19105, 1969.

PRACTICAL UROLOGY. By Chester C. Winter, M.D., F.A.C.S., Professor of Urology, The Ohio State University College of Medicine; Director of Urology, University Hospitals, Columbus, Ohio. Cloth. Pp. 250, with 251 illustrations. Price, $11.00. C. V. Mosby Company, Publishers, 3207 Washington Blvd., St. Louis, Mo. 63103, 1969.

PULMONARY EMPHYSEMA AND RELATED LUNG DISEASES. By Theodore Rodman, M.D., Associate Professor of Medicine, Temple University School of Medicine; formerly, Chief, Cardiopulmonary Laboratory, Philadelphia Veterans Administration Hospital, Philadelphia, Pa.; and Francis H. Sterling, M.D., Associate in Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pa. Cloth. Pp. 468, with 294 illustrations. Price, $27.50. C. V. Mosby Company, Publishers, 3207 Washington Blvd., St. Louis, Mo. 63103, 1969.

BASIC DIAGNOSTIC RADIOLOGY: AN INTRODUCTORY TEXTBOOK FOR STUDENTS IN THE MEDICAL SCIENCES. By Malcolm D. Jones, M.D., Professor and Vice-Chairman, Department of Radiology; Professor of Radiology, Division of Ambulatory and Community Medicine, University of California Medical School, San Francisco, Calif. Cloth. Pp. 266, with 511 illustrations. Price, $11.75, C. V. Mosby Company, Publisher, 3207 Washington Blvd., St. Louis, Mo. 63103, 1969.

THE LUNGS IN SYSTEMIC DISEASES. By Eli H. Rubin, M.D., F.A.C.P., F.C.C.P., Professor of Clinical Medicine, Albert Einstein College of Medicine, Yeshiva University; Attending Physician, Division of Pulmonary Medicine, Montefiore Hospital and Medical Center; Visiting Physician, Chest Service, Bronx Municipal Hospital Center; Consulting Physician, Bronx-Lebanon Hospital Center and Morrisania City Hospital, New York, N. Y.; and Stanley S. Siegelman, M.D., Assistant Professor of Radiology, Albert Einstein College of Medicine, Yeshiva University; Associate Attending Physician, Division of Diagnostic Roentgenology, Montefiore Hospital and Medical Center, New York, N. Y. Cloth. Pp. 312, with many illustrations. Price, $20.75. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62703, 1969.

THE PHYSICS OF RADIOLOGY. Third edition. By Harold Elford Johns, M.A., Ph.D., F.R.S.C., LL.D., Professor and Head of the Department of Medical Biophysics; Professor of Physics, University of Toronto; Head, Physics Division, Ontario Cancer Institute, Toronto, Ont., Canada; and John Robert Cunningham, B. Eng., M.Sc., Ph.D., Senior Clinical Physicist, Ontario Cancer Institute; Assistant Professor, Department of Medicial Biophysics, University of Toronto. Cloth. Pp. 800, with some figures. Price, $24.75. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62703, 1969.

MOTOR NEURON DISEASES: RESEARCH ON AMYOTROPHIC LATERAL SCLEROSIS AND RELATED DISORDERS. Contemporary Neurology Symposia, Volume II. Dedicated to the memory of Lord Brain. Edited by Forbes H. Norris, Jr., and Leon-

ard T. Kurland. Cloth. Pp. 407, with some illustrations. Price, $13.25. Grune & Stratton, Inc., 381 Park Avenue South, New York, N. Y. 10016, 1969.

Celiac and Superior Mesenteric Arteries: A Correlation of Angiograms and Dissections. By Robert A. Nebesar, M.D., Instructor in Radiology, Harvard Medical School; Associate in Radiology, Children's Hospital Medical Center; Clinical Associate in Radiology, Massachusetts General Hospital, Boston; Paul L. Kornblith, M.D., Research Fellow in Surgery, Harvard Medical School; Massachusetts General Hospital, Boston; James J. Pollard, M.D., Instructor in Radiology, Harvard Medical School; Assistant Radiologist, Massachusetts General Hospital, Boston; and Nicholas A. Michels, D.Sc., Professor of Anatomy, Emeritus, at the Daniel Baugh Institute of Anatomy, Jefferson Medical College, Philadelphia. Cloth. Pp. 226, with many illustrations. Price, $16.00. Little, Brown and Company, 34 Beacon Street, Boston, Mass. 02106, 1969.

Pneumomyelography. By Jan Jirout, M.D., Dr.Sc., Professor, Department of Radiology, Neurologic Clinic, Prague, Czechoslovakia. Translated and edited by John A. Goree, M.D., Associate Professor of Radiology, Duke University School of Medicine, Durham, N. C. Cloth. Pp. 276, with many illustrations. Price, $18.00. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62703, 1969.

Annual Review of Medicine. Arthur C. DeGraff, Editor, New York University School of Medicine; William P. Creger, Associate Editor, Stanford University School of Medicine. Volume 20. Cloth. Pp. 500. Price, $8.50, U.S.A., $9.00 Foreign. Annual Reviews, Inc., 4139 El Camino Way, Palo Alto, Calif. 94306, 1969.

SOCIETY PROCEEDINGS

MEETINGS OF RADIOLOGICAL SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. Ted F. Leigh, Emory University Clinic, Atlanta, Ga. 30322. Annual Meeting: Washington-Hilton Hotel, Washington, D.C., September 30–October 3, 1969.

AMERICAN RADIUM SOCIETY
Secretary, Dr. John V. Blady, The Parkway House, 2201 Benjamin Franklin Parkway, Philadelphia, Pa. 19130. Annual meeting: Hotel Coronado, San Diego, Calif., March 1–6, 1970.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary-Treasurer, Dr. Maurice Doyle Frazer, 1744 South Fifty-eighth St., Lincoln, Neb. Annual meeting: Palmer House, Chicago, Ill., November 30–December 5, 1969.

AMERICAN COLLEGE OF RADIOLOGY
Executive Director, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Ill. Annual meeting: Statler-Hilton Hotel, Dallas, Tex., March 31–April 4, 1970.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. Kenneth L. Krabbenhoft, Harper Hospital, Detroit, Mich. 48201. Annual meeting: New York, N. Y., July 13–17, 1969.

AMERICAN BOARD OF RADIOLOGY
Secretary, Dr. C. Allen Good. Correspondence should be directed to Kahler Center Building, Rochester, Minn. 55901.
The oral examination will be held at the Statler Hilton Hotel, Dallas, Texas, Dec. 8–12, inclusive, 1969.
The deadline for filing applications for the above examination was December 31, 1968.

AMERICAN ASSOCIATION OF PHYSICISTS IN MEDICINE
Secretary, Leonard Stanton, Hahnemann Medical College, 230 N. Broad St., Philadelphia, Pa. 19102.

AMERICAN SOCIETY OF THERAPEUTIC RADIOLOGISTS
Secretary, Dr. Carl R. Bogardus, Jr., University of Oklahoma Medical Center, Oklahoma City, Oklahoma 73104

AMERICAN SOCIETY FOR DIAGNOSTIC ULTRASOUND
Secretary, Dr. Charles C. Grossman, 552 N. Neville St., Pittsburgh, Pa. 15213.

AMERICAN SOCIETY OF NEURORADIOLOGY
Secretary-Treasurer, Dr. Alan E. Zimmer, Danbury, Conn. 06810.

TWELFTH INTERNATIONAL CONGRESS OF RADIOLOGY
President, Dr. Kempo Tsukamoto, 9-1, 4-chome, Angewa, Chiba, Japan. Meeting: Hotel New Otani, Tokyo, Japan, Oct. 6–11, 1969.

TENTH INTER-AMERICAN CONGRESS OF RADIOLOGY
Counselor for the United States, Dr. Juan A. del Regato, Penrose Cancer Hospital, 2215 North Cascade Ave., Colorado Springs, Colo. 80907.
President, Dr. Juan A. del Regato, Colorado Springs, Colo., USA.
Secretary, Dr. F. Bloedorn, Boston, Mass., USA.
Meeting: San Juan, Puerto Rico, 1971.

INTER-AMERICAN COLLEGE OF RADIOLOGY
President, Dr. Oscar Soto, H. Urteaga 480, Lima, Perú.

ALABAMA RADIOLOGICAL SOCIETY
Secretary, Dr. William V. Weldon, Medical Arts Building, Birmingham, Ala. 35205. Meets time and place of Alabama State Medical Association.

ALASKA RADIOLOGICAL SOCIETY
Secretary, Dr. Bruce C. Wright, Providence Hospital, Anchorage, Alaska. Meets third Wednesday each month.

ARIZONA RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Robert E. Steyskal, 550 W. Thomas Rd., Phoenix, Ariz. 85013. Two regular meetings a year. Annual meeting at time and place of State Medical Association and interim meeting six months later.

ARKANSAS CHAPTER OF AMERICAN COLLEGE OF RADIOLOGY
Secretary-Treasurer, Dr. Wilma C. Diner, Univ. of Arkansas Medical Center, Little Rock, Ark. 72201.

ARKANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Charles W. Anderson, 1108½ Poplar, Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

ASSOCIATION OF UNIVERSITY RADIOLOGISTS
Secretary-Treasurer, Dr. James J. Scatliff, University of North Carolina Medical School, Chapel Hill, N. C. 27514. Annual Meeting: University of Kentucky Medical Center, Lexington, Ky., April 29–May 1, 1970.

ATLANTA RADIOLOGICAL SOCIETY
Secretary, Dr. Donald R. Rooney, Burnt Hickory Road, Marietta, Ga. Meets monthly except during three summer months, on third Tuesday, at the Academy of Medicine, Atlanta, Ga., at 8:00 P.M.

BAVARIAN-AMERICAN RADIOLOGIC SOCIETY
Advisor, Colonel Paul E. Sieber. *Secretary*, Major Peter B. Riesz, USAH Bad Cannstatt, APO 09154, New York, N. Y. Meets quarterly.

BLOCKLEY RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. R. John Gould, 41 Lombardy Rd., Drexel Hill, Pa. 19026.

BLUEGRASS RADIOLOGICAL SOCIETY
Secretary-Treasurer, Joseph A. Sayeg, Ph.D., Radiation Physicist, University of Kentucky, Lexington, Kentucky 40506. The Society meets once each month during the school year.

BROOKLYN RADIOLOGICAL SOCIETY
Secretary, Dr. Coleman H. Rosenberg, 81–10 Chevy Chase St., Jamaica, N.Y. 11432. Meets first Thursday of each month, October through June.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Herbert Pirson, 145 High Park Blvd., Buffalo, N. Y. 14226. Meets second Monday evening each month, October to May inclusive., at University Club.

CALIFORNIA RADIOLOGICAL SOCIETY
Secretary-Treasurer: Dr. Leroy K. Mills, 3157 Oakcliff Circle, Carmichel, Calif. 95608. Meets annually during meeting of California Medical Association.

CATAWBA VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. Emmett R. White, P. O. Box 303, Rutherford College, N. C. 28671. Meets every Friday, Dept. of Radiology, Valdese General Hosp., Valdese, N. C., at 12:00 NOON.

CENTRAL NEW YORK RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. David N. Cheris, Community General Hospital of Greater Syracuse, Broad Road, Syracuse, N. Y. 13215. Meets first Monday each month, October through May.

CENTRAL OHIO RADIOLOGICAL SOCIETY
Secretary, Dr. Ollie E. Southard, 2787 Tudor Rd., Columbus, O. 43209. Meets second Thursday in October, November, January, and March 15 and May 19 at Fort Hayes Hotel, Columbus, Ohio.

*** Secretaries of societies are requested to send timely information promptly to the Editor.**

Chicago Roentgen Society
Secretary-Treasurer, Dr. Howard C. Burkhead, 2650 Ridge Ave., Evanston, Ill. 60202. Meets third Wednesday of each month, October to April, except December, at the University Club of Chicago.

Cleveland Radiological Society
Secretary-Treasurer, Dr. James Farmer, 18869 Canyon Rd. Fairview Park, Ohio 44126. Meetings at 7:00 P.M. on fourth Monday of October, November, January, February, March and April.

Colorado Radiological Society
Secretary, Dr. Charles E. Seibert, Department of Radiology, Swedish Hospital, 501 E. Hampton, Englewood, Colo. 80110. Meets third Friday of each month at Denver Athletic Club from September through May.

Connecticut Valley Radiologic Society
Secretary, Dr. William W. Walthall, Jr., 130 Maple St., Springfield, Mass. Meets in April and October.

Dallas-Fort Worth Radiological Society
Secretary-Treasurer, Dr. R. W. Perrin, P.O. Box 5999, Dallas, Texas 75222. Meets the 3rd Monday of every month at 6:30 P.M., at the Cibola Inn, Arlington, Texas.

Detroit Roentgen Ray Society
Secretary, Dr. David P. Corbett, Harper Hospital, Detroit, Mich. 48201. Meets monthly, first Thursday, October through May, at David Whitney House, 1010 Antietam, at 6:30 P.M.

East Bay Radiological Society
Secretary, Dr. Burke L. Winget, Samuel Merritt Hospital, 34th Webster Street, Oakland, Calif. 94609. Meets first Thursday each month, Oct. through May, at University Club, Oakland, Calif.

East Tennessee Radiological Society
Secretary-Treasurer, Dr. Eberhard F. Besemann, Baroness Erlanger Hospital, Chattanooga, Tenn. 37403. Meets in January and September.

Florida Radiological Society
Secretary, Dr. Robert H. Nickau, Good Samaritan Hospital, West Palm Beach, Fla. 33402. Meets twice annually, in the spring with the annual State Society Meeting and in the fall.

Florida West Coast Radiological Society
Secretary-Treasurer, Dr. Allen L. Sheer, University Community Hospital, 13505 N. 31st St., Tampa, Fla. 33612. Meets in January, March, May, July, September and November.

Georgia Radiological Society
Chapter of the American College of Radiology
Secretary, Dr. Walker Harris, The Medical Center, Columbus, Georgia 31902. Meets in spring and fall at Annual State Society Meeting.

Greater Cincinnati Radiological Society
Secretary-Treasurer, Dr. Owen L. Brown, 2421 Auburn Ave., Cincinnati, Ohio 45219.

Greater Louisville Radiological Society
Secretary-Treasurer, Dr. L. D. LeNeave, 315 E. Broadway, Louisville, Ky. 40202. Meets monthly.

Greater Miami Radiological Society
Secretary-Treasurer, Dr. Sylvan H. Sarasohn, P. O. Box 1256, North Miami, Fla. 33161. Meets monthly, third Wednesday at 8:00 P.M. at Jackson Memorial Hospital, Miami, Fla.

Greater St. Louis Society of Radiologists
Secretary-Treasurer, Dr. Roland P. Ernst, 3720 Washington Ave., St. Louis, Mo. 63108.

Hawaii Radiological Society
Secretary-Treasurer, Dr. Thomas C. Brown, 1697 Ala Moana Blvd., Honolulu, Hawaii 96815. Meets third Monday of each month at 7:30 P.M.

Health Physics Society
Secretary, R. J. Augustine, National Center for Radiologic Health, 1901 Chapman Ave., Rockville Md. 20852.

Houston Radiological Society
Secretary, Dr. Eleanor Montague, 6516 Bertner, Houston, Tex. 77025. Meets fourth Monday of each month, except June, July, August and December, at 6:00 P.M., at 103 Jesse H. Jones Library Building, Texas Medical Center, Houston, Tex. 77025.

Idaho State Radiological Society
Secretary, Dr. George H. Harris, Bannock Memorial Hospital, Pocatello, Idaho. Meets in the spring and fall.

Illinois Radiological Society, Inc.
Secretary, Dr. C. R. Markivee, 674 North Seminary St., Galesburg, Ill. 61401. Meets in the spring and fall.

Indiana Roentgen Society, Inc.
Secretary, Dr. Edwin F. Koch, Jr., 915 University Ave., Muncie, Ind. 47303. Meets first Sunday in May and during fall meeting of Indiana State Medical Association.

Iowa Radiological Society
Secretary-Treasurer, Dr. J. H. Lohnes, 1948 First Ave., N.E., Cedar Rapids, Iowa 52402. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

Kansas Radiological Society
Secretary-Treasurer, Dr. Robert C. Lawson, 310 Medical Arts Bldg., 10th and Horne, Topeka, Kan. Meets in spring with State Medical Society and in winter on call.

Kentucky Chapter, American College of Radiology
Secretary-Treasurer, Dr. Ralph C. Quillin, 1221 S. Broadway, Lexington, Ky. 40504. Meets in April and September.

Kings County Radiological Society
Secretary, Dr. Sidney Hendler, 1880 Ocean Ave., Brooklyn 30, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Knoxville Radiological Society
Secretary, Dr. Clifford L. Walton, Blount Professional Bldg., Knoxville 20, Tenn. Meetings are held the third Monday of every other month at the University of Tennessee Memorial Research Center and Hospital.

Long Island Radiological Society
Secretary, Dr. Robert J. Hochstim, 1200 Stewart Ave., Garden City, N. Y. 11533. Meets monthly.

Los Angeles Radiological Society
Secretary, Dr. John L. Gwinn, Childrens Hospital of Los Angeles, 4650 Sunset Blvd., Los Angeles, Calif. 90027. Meets second Wednesday of month in September, November, January, April and June at Los Angeles County Medical Association Building, Los Angeles, Calif.

Louisiana-Texas Gulf Coast Radiological Society
Secretary-Treasurer, Dr. Edward A. Sheldon, 109 Doctors Bldg., Beaumont, Texas 77701.

Maine Radiological Society
Secretary-Treasurer, Dr. Robert A. Bearor, Maine Medical Center, Portland, Maine 04102. Meets in June, September, December and April.

Maryland Radiological Society
Secretary, Dr. Nathan Stofberg, 4519 Hawksbury Rd., Pikesville, Md. 21208.

Massachusetts Radiological Society
Secretary, Dr. Jerome H. Shapiro, Department of Radiology, Boston City Hospital, 818 Harrison Ave., Boston, Mass. 02118.

Memphis Roentgen Society
Secretary-Treasurer, Dr. Webster Riggs, Jr., The University of Tennessee College of Medicine, Department of Radiology, Walter F. Chandler Bldg., 865 Jefferson Ave., Memphis, Tenn. 38103. Meets first Monday of each month at John Gaston Hospital.

Miami Valley Radiological Society
Secretary, Dr. Darwood B. Hance, Reid Memorial Hospital, Richmond, Indiana. Meets third Thursday of fall, winter and spring months at 7:30 P.M. at Miami Valley Hospital, Dayton, Ohio.

Mid-Hudson Radiological Society
Secretary-Treasurer, Dr. Herbert S. Berlin, Hopewell Junction, N. Y. Meets 7:00 P.M., first Wednesday of each month, September to May.

Milwaukee Roentgen Ray Society
Secretary-Treasurer, Dr. James E. Bell, 8700 W. Wiscon-

sin Ave., Milwaukee, Wis. 53213. Meets monthly on fourth Monday, October through May, at University Club.

Minnesota Radiological Society
Secretary-Treasurer, Dr. Warren L. Kump, 4243 Glenwood Ave., Minneapolis, Minn. 55422. Meets twice annually, fall and winter.

Mississippi Radiological Society
Secretary-Treasurer, Dr. Ottis G. Ball, 5356 Balmoral Drive, Jackson, Miss. 39211. Meets third Thursday of each month at the Heidelberg Hotel, Jackson, at 6:00 P.M.

Missouri Radiological Society
Secretary-Treasurer, Dr. Arthur A. Porporis, 100 N. Euclid Ave., St. Louis, Mo. 63108.

Montana Radiological Society
Secretary, Dr. Colvin H. Agnew, Doctors' Building, 1231 N. 29th Street, Billings, Montana 59101. Meets in Glacier National Park, July 23–25, 1969.

Nebraska State Radiological Society
Secretary-Treasurer, Dr. Otto A. Troester, 924 Sharp Building, Lincoln, Nebraska 60508. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

Nevada Radiological Society
Secretary, Dr. William G. Arbonies, Department of Radiology, St. Mary's Hospital, Reno, Nev.

New England Roentgen Ray Society
Secretary, Dr. Morris Simon, 330 Brookline Ave., Boston, Mass. 02115. Meets third Friday of each month, October through May, at The Longwood Towers, 20 Chapel Street, Brookline, Mass., at 4:30 P.M.

New Hampshire Roentgen Ray Society
Secretary, Dr. Paul Y. Hasserjian, 1470 Elm St., Manchester, N. H. Meets four to six times yearly.

New Mexico Association of Radiologists
Secretary-Treasurer, Dr. Justin J. Wolfson, Department of Radiology, Bernalillo County-Indian Hospital, Albuquerque, New Mexico.

New Mexico Society of Radiologists
Secretary, Dr. Donald A. Wolfel, Albuquerque, New Mexico. Four meetings annually, three held in Albuquerque, N. M., and one held at time and place of New Mexico State Medical Society annual meeting.

New York Roentgen Society
Secretary-Treasurer, Dr. Samuel H. Madell, 1 E. 82nd St New York, N. Y. 10024. Meets monthly on third Monday at the New York Academy of Medicine at 4:30 P.M.

New York State Chapter of the American College of Radiology, Inc.
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester, N. Y., 14618.

North Carolina Chapter of ACR.
Secretary-Treasurer, Dr. James F. Martin, 300 S. Hawthorne Road, Winston-Salem, N.C. 27103.

North Carolina Radiological Society
Secretary, Dr. E. H. Schultz, North Carolina Memorial Hospital, Chapel Hill, N. C. Meets in the spring and fall each year.

North Dakota Radiological Society
Secretary, Dr. A. Ohrt, 408 Medical Arts Bldg., Fargo, N. D. 58102. Meets at time of State Medical Association meeting. Other meetings arranged on call of the President.

North Florida Radiological Society
Secretary, Dr. Charles H. Newell, 800 Miami Road, Jacksonville 7, Fla. Meets quarterly in March, June, September and December.

Northeastern New York Radiological Society
Secretary, Dr. Herbert F. Reilly, Jr., 12 Sandalwood Rd., Scotia, New York 12302. Meets in Albany area on third Wednesday of October, November, March, April, and May.

Northern California Radiological Society
Secretary-Treasurer, Ivan D. Siddons, 3701 J. St., Suite 106, Sacramento, Calif. 95816. Meets fourth Monday of Sept., Nov., Jan., March and May at the Sutter Club in Sacramento.

Northwestern Ohio Radiological Society
Secretary, Dr. Vito J. Zupa, Mercy Hospital, Department of Radiology, Toledo, Ohio.

Ohio State Radiological Society
Secretary, Dr. Robert D. Berkebile, Elyria Memorial Hospital, Elyria, Ohio 44035.

Oklahoma State Radiological Society
Secretary, Dr. Donald F. Mauritson, 100 Utica Square Med. Center, Tulsa, Okla. 74114. Meets in January, May and October.

Orange County Radiological Society
Secretary, Dr. Richard Simpson, Hoag Memorial Hospital, 301 Newport Ave., Newport Beach, California. Meets on fourth Tuesday of the month, excluding June, July, August, and December, at the Orange County Medical Association Bldg., Orange, Calif.

Oregon Radiological Society
Secretary-Treasurer, Dr. Clinton B. Sayler, 214 Medical Dental Bldg., Portland, Oregon 97205. Meets on second Wednesday of month, October through April, at the University Club, Portland, Ore.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans, La. 70113. Meets second Tuesday of each month.

Pacific Northwest Radiological Society
Secretary-Treasurer, Dr. Marvin Wallace, 555 108th Ave. N. E., Bellevue, Washington 98004.

Pennsylvania Radiological Society
Secretary, Dr. Theodore A. Tristan, Harrisburg, Polyclinic Hosp., Harrisburg, Pa. 17105.

Philadelphia Roentgen Ray Society
Secretary, Dr. C. Jules Rominger, Misericordia Hospital, 54th St. and Cedar Ave., Philadelphia, Pa. 19143. Meets first Thursday of each month at 5 P.M., from October to May in Thompson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. Edward R. Seitz, 601 Jenkins Bldg., Pittsburgh, Pa. 15222. Meets second Wednesday of month, October through June, at Park Schenley Restaurant.

Radiation Research Society
Secretary-Treasurer, Dr. Gail D. Adams, Dept. of Radiology, Univ. of Oklahoma Medical Center, Oklahoma City, Oklahoma 73104.

Radiological Society of Connecticut, Inc.
Secretary-Treasurer. Dr. Henry J. Fox, 10 Washington Ave., Bridgeport, Conn. Meetings are held quarterly.

Radiological Society of Greater Cincinnati
Secretary-Treasurer, Dr. Donald E. Gunderson, 3553 Bayard Dr., Cincinnati, Ohio 45208. Meets first Monday of each month at Cincinnati Academy of Medicine.

Radiological Society of Greater Kansas City
Secretary, Dr. Leo G. Goertz, 155 S. 18th St., Kansas City, Kans. 66102. Meets last Friday of each month.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Radiological Society of Louisiana
Secretary, Dr. Lester W. Eavenson, 2700 Napoleon Ave., New Orleans 15, La. Meets semiannually, during Louisiana State Medical Society meeting and 6 months later.

Radiological Society of New Jersey
Secretary, Dr. John W. Marquis, 12 Hawthorne Ave., East Orange, N. J. 07018. Meets in Atlantic City at time of State Medical Society meeting and in October or November in Newark, N. J.

Radiological Society of Rhode Island
Secretary-Treasurer, Dr. John M. Vesey, 1196 Elmwood Ave., Cranston, R. I.

Radiological Society of South Dakota
Secretary-Treasurer, Dr. Donald J. Peik, 303 S. Minnesota Ave., Sioux Falls, S. D.

Radiological Society of Southern California
Secretary-Treasurer, Dr. Robert G. Williams, The Santa Barbara Medical Clinic, P.O. Box 1200, Santa Barbara, Calif. 93102. Meets three times a year, usually October, February and May.

Radiological Society of the State of New York
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester, N. Y. 14618.

Redwood Empire Radiological Society
Secretary, Dr. Lee F. Titus, 164 W. Napa St., Sonoma, Calif. Meets second Monday every other month.

Richmond County Radiological Society
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga. Meets first Thursday of each month at various hospitals.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Kenneth E. Robinson, Rochester General Hospital, 1425 Portland Ave., Rochester, N. Y. 14621. Quarterly meetings on the call of the President, at the Rochester Academy of Medicine.

Rocky Mountain Radiological Society
Secretary-Treasurer, Dr. Robert W. Lackey, 4200 E. Ninth Ave., Denver, Colo. 80220. Annual meeting: Brown Palace Hotel, Denver, Colo., Aug. 21–23, 1969.

San Antonio-Military Radiological Society
Secretary, Dr. Hugho F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Tex. Meets third Wednesday of each month in Fort Sam Houston Officer's Club at 6:30 P.M.

San Diego Radiological Society
President-Secretary, Charles R. Henkelmann, 3909 Palm Drive, Bonita, Calif. 92002. Meets first Wednesday of each month at the Town & Country Motel.

San Francisco Radiological Society
Secretary-Treasurer, Dr. Warren M. Russell, Franklin Hospital, Castro & Duboce, San Francisco, Calif. 94114. Meets quarterly at various hospitals (contact Secretary).

Santa Clara County Radiological Society
Secretary, Dr. John J. Berg, 45 So. 17th Street, San Jose, Calif. 95112. Meets monthly at the Santa Clara County Medical Association Bldg., 700 Empey Way, San Jose, Calif.

Section on Radiology, California Medical Association
Secretary, Dr. William H. Graham, 630 East Santa Clara St., San Jose, Calif.

Section on Radiology, Medical Society of the District of Columbia
Secretary-Treasurer, Dr. Louis Wener, Cafritz Memorial Hosp., 1310 Southern Ave., S.E., Washington, D. C. 20032. Meets at Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

Section on Radiology, Southern Medical Association
Secretary, Dr. Phillip W. Voltz, Jr., 120 Medical Professional Bldg., San Antonio, Texas 78212. Annual meeting: To be announced.

Section on Radiology, Texas Medical Association
Secretary, Dr. George F. Crawford, St. Elizabeth Hospital, Beaumont, Tex. Meets annually with the Texas Medical Association.

Shreveport Radiological Club
Secretary, Dr. W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday at 7:30 P.M., September to May inclusive.

Society for Pediatric Radiology
Secretary, Dr. John L. Gwinn, Children's Hospital, 4614 Sunset Blvd., Los Angeles 27, Calif. Annual meeting: Washington-Hilton Hotel, Washington, D.C., September 29, 1969.

Society of Nuclear Medicine
Secretary, Mr. C. Craig Harris, Oak Ridge National Laboratories, Oak Ridge, Tenn. *Administrator*, Mr. Samuel N. Turiel, 430 N. Michigan Ave., Chicago 11, Ill.

South Bay Radiological Society
Secretary, Dr. Emerson C. Curtis, University Dr., Menlo Park, Calif. 94025. Meets second Wednesday of each month.

South Carolina Radiological Society
Secretary, Dr. George W. Brunson, 1406 Gregg St., Columbia, S. C. Annual meeting (primarily business) in conjunction with the South Carolina Medical Association meeting in May. Annual fall scientific meeting at time and place designated by the president.

South Dakota Radiological Society
Secretary, Dr. Donald J. Peik, 1417 S. Minnesota Ave., Sioux Falls, S. Dak. Meets in spring with State Medical Society and in fall.

Southern California Radiation Therapy Society
Secretary-Treasurer, Dr. Aaron G. Fingerhut, 1000 W. Carson St., Torrance, Calif. 90502. Meets quarterly.

Southern Radiological Conference
Secretary-Treasurer, Dr. Marshall Eskridge, Mobile Infirmary, P.O. Box 4097, Mobile, Ala. 36604. Annual meeting: Grand Hotel, Pointe Clear, Ala. 36564, Jan. 30–Feb. 1, 1970.

Southwestern Radiological Society
Secretary, John M. McGuire, 904 Chelsea, El Paso, Tex. Meets last Monday of each month at 6:30 P.M. in the Paso del Norte Hotel.

Tennessee Radiological Society
Secretary-Treasurer, Dr. Lawrence R. Nickell, Maury County Hospital, Columbia, Tennessee 38401. Meets annually at the time and place of the Tennessee State Medical Association meeting.

Texas Radiological Society
Secretary, Dr. Herman C. Sehested, 815 Medical Arts Bldg., Fort Worth 2, Tex. Annual meeting to be announced.

Tri-State Radiological Society
Secretary, Dr. John H. Marchand, Jr., Methodist Hospital, Henderson, Ky. Meets third Wednesday of Oct., Jan., March and May, 8:00 P.M., Elks Club in Evansville, Ind.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital, Ann Arbor Mich.

Upper Peninsula Radiological Society
Secretary, Dr. A. Gonty, Menominee, Mich. Meets quarterly.

Utah State Radiological Society
Secretary-Treasurer, Dr. Leon M. Neal, St. Benedict's Hospital, 3000 Polk Ave., Ogden, Utah 84403. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

Vermont Radiological Society
Secretary, Dr. John R. Williams, 160 Allen St., Rutland, Vt.

Virginia Radiological Society
Secretary-Treasurer, Dr. K. Kenneth Wallace, Jr., Virginia Beach, Va.

Washington State Radiological Society
Secretary-Treasurer, Dr. Paul S. Paulson, 1001 Broadway, Seattle, Washington 98122. Meets quarterly.

West Virginia Radiological Society
Secretary-Treasurer, Dr. George G. Green, Department of Radiology, W. Va. Univ. Medical Center, Morgantown, W. Va. 26506. Meets concurrently with Annual Meeting of West Virginia State Medical Society; other meetings arranged by program committee.

Westchester County Radiological Society
Secretary, Dr. Edgar Palmer, 650 Main St., New Rochelle, N. Y. 10801.

Meets on third Tuesday of January and October and on two other dates.

Wisconsin Radiological Society
Secretary-Treasurer, Dr. Robert E. Douglas, 117 N. Commercial St., Neenah, Wis. 54956. Meets twice a year, May and September.

Wyoming Radiological Society
Secretary, Dr. J. D. Grant, Memorial Hosp., Sheridan, Wyo. Meets in fall with State Medical Society and in spring on call of President.

Mexico, Puerto Rico and Central America

Asociación Costariccense de Radiología
Secretary, Dr. Jorge Vargas Segura, Apartado 5367, San José, Costa Rica.

Asociación de Radiólogos de Centro America y Panamá. Comprising: Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica and Panamá.
Secretary-General, Dr. Roberto Calderón, Calle Central Oeste No. 218, Managua, Nicaragua, Central America. Meets annually in a rotating manner in the six countries.

Sociedad de Radiología de El Salvador
Secretary, Dr. Julio Astacio, 5a Av. Nte. No. 434, San Salvador, Rep. El Salvador.

Sociedad de Radiología de Guatemala
Secretary, Dr. Carlos E. Escobar, 9ª. Calle A 0-05, Zona 1, Guatemala.

Sociedad Mexicana de Radiología, A.C.
Coahuila No. 35, México 7, D. F.
Secretary-General, Dr. Ramón Ruenes.
Meets first Monday of each month.

Asociación Puertorriqueña de Radiología
Secretary, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, Puerto Rico.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sánchez, Apartado No. 6323, Panamá, R. de P. Meets monthly in a department of radiology of a local hospital chosen at preceding meeting.

Sociedad Radiológica de Puerto Rico
Secretary, Dr. Felipe N. de Jesús, Apt. 9387, Santurce, Puerto Rico. Meets second Thursday of each month at 8:00 P.M. at the Puerto Rico Medical Association Bldg. in San Juan.

British Commonwealth of Nations

Association of Radiologists of the Province of Quebec
Secretary, Dr. R. Robillard, Notre-Dame Hospital, 1560 Sherbrooke St., East, Montreal, Que., Canada. Meets four times a year.

British Institute of Radiology
Honorary Secretary, Dr. G. H. du Boulay, 32 Welbeck St., London, W. 1, England. Meets monthly from October until May.

Canadian Association of Physicists, Division of Medical and Biological Physics.
Honorary Secretary-Treasurer, Paul M. Pfalzner, Department of Therapeutic Radiology, University of Western Ontario, London, Ontario, Canada.

Edmonton and District Radiological Society
Secretary, J. D. R. Miller, M.B., University of Alberta Hospital, Edmonton, Alberta, Canada. Meets third Thursday of each month October to May, except December, at various Edmonton Hospitals.

Faculty of Radiologists
Honorary Secretary, Dr. J. N. Pattinson, 47 Lincoln's Inn Fields, London, W.C.2, England.

Faculty of Radiologists, Royal College of Surgeons in Ireland
Registrar, Dr. H. O'Flanagan, F.R.C.P.I., D.P.H., 123 St. Stephens Green, Dublin 2, Ireland.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1, England.

Canadian Association of Radiologists
Honorary Secretary-Treasurer, Dr. Maurice Dufresne, *Associate Honorary Secretary-Treasurer*, Dr. F. Robert MacDonald, 1555 Summerhill Ave., Montreal 25, Que., Canada. Annual Meeting: To be announced.

Montreal Radiological Study Club
Secretary, Dr. Leonard Rosenthall, Montreal General Hospital, Montreal, Que., Canada. Meets first Tuesday evening, October to April.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française de Radiologie
Secretary General, Dr. Guy Duckett, 1385 est, rue Jean Talon, Montréal P.Q., Canada. Meets every third Tuesday from October to April, Annual Meeting: Nov. 6–8, 1969.

Toronto Radiological Society
Secretary, Dr. George Wortzman, Toronto General Hosp., Toronto 12, Ont., Canada. Meets second Monday of each month, September through May.

College of Radiologists of Australasia
Honorary Secretary, Dr. T. P. Loneragan, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W., Australia.

South America

Asociación Argentina de Radiología
Secretary, Dr. Lidio G. Mosca, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

Ateneo de Radiologia
Secretary, Dr. Victor A. Añaños, Instituto de Radiologia, Santa Fe 3100, Rosario, Argentina. Meets monthly on second and fourth Fridays at 7:00 P.M. in the Hospital Nacional de Centenario, Santa Fe 1300, Rosario.

Colégio Brasileiro de Radiologia
Secretary-General, Dr. Miguel Mario Céntola, Caixa Postal 5984, São Paulo, Brazil.

Sociedad Argentina de Radiología
Secretary-General, Dr. Juan R. Heilbuth, Pacheco, Santa Fe 1171, Buenos Aires. Meets First Wednesday evening, April through December.

Sociedad Boliviana de Radiología
Secretary, Dr. Javier Prada Méndez Casilla 1182, La Paz, Bolivia. Meets monthly. General assembly once every two years.

Sociedade Brasileira de Radiologia
Secretary, Dr. Armando Rocha Amoédo, Cxa Postal 1532, Rio de Janeiro, Brazil. General Assembly meets every two years in December.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Chilena de Radiología
Secretary, Dr. Manuel Concha, Casilla 13426, Santiago, Chile. Meets fourth Friday of each month.

Sociedad Colombiana de Radiologia
Secretary-General, Dr. Armando Uribe, Hospital Militar Central, Apartado aéreo No. 5804, Bogotá, Colombia. Meets last Thursday of each month.

Sociedad Ecuatoriana de Radiología y Fisioterapía
Secretary, Dr. Carlos Palau, Av. Bogotá 206, Guayaquil, Ecuador.

Sociedad Paraguaya de Radiología
Secretary, Dr. Miguel González Addone, 15 de Agosto 322, Asunción, Paraguay.

Sociedad Peruana de Radiologia
Secretary-General, Dra. Ladis Delpino, Instituto de Radiología "Cayetano Heredia" Hospital Arzobispo Loayza, Lima, Perú. Meets monthly except during January, February and March.

Sociedad de Radiologica del Atlantico
Secretary, Dr. Raul Fernandez, Calle 40 #41–110, Baran-

quilla, Colombia. Society meets monthly at the Instituto de Radiología.

Sociedad de Radiología, Cancerología y Física Médica del Uruguay
Secretary-General, Dr. José Claussius, Av. Agraciada 1464, piso 13, Montevideo, Uruguay.

Sociedade de Radiología de Pernambuco
Secretary, Dr. Manoel Medeiros, Instituto de Radiologia da Faculdade de Medicina da Universidade do Recife, Caixa Postal 505, Pernambuco, Brazil.

Sociedad de Roentgenología y Medicina Nuclear de la Provincia de Córdoba
Secretary-General, Dr. Lucas C. Di Rienzo, Ave. Grl. Paz. 151, Córdoba, Argentina.

Sociedad Venezolana de Radiología
Secretary-General, Dr. Modesto Rivero Gonzáles, Apartado No. 9362 Candelaria, Caracas, Venezuela. Meets monthly, third Friday at Colegio Médico del Distrito Federal, Caracas.

Continental Europe

Österreichische Röntgen-Gesellschaft
President, Dr. Konrad Weiss, Mariannengasse 10, Vienna 9, Austria. Meets second Tuesday of each month in Allgemeine Poliklinik.

Société Royale Belge de Radiologie
General Secretary, Dr. Joseph Baeyens, Alost, Belguim. Meets in February, March, May, June, September, October, November and December.

Société Européenne de Radiologie Pédiatrique
Permanent Secretary, Dr. Jaques Sauvegrain, Hôpital des Enfants-Malades, 149, rue de Sèvres, Paris 15e, France.
General Secretary, Dr. H. Ludin, Department of Roentgenology, Basler Kinderspital, Basel, Switzerland.

Société Française d'Electroradiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, du Nord, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord. Central Society meets third Monday of each month, except during July, August and September, rue de Seine 12, Paris, France.
Secretary-General, Dr. Ch. Proux, 9 rue Daru Paris 8e, France.

Československá Společnost pro Roentgenologii a Radiologii
Secretary, Dr. Robert Poch, Praha 12, Srobárova 50, Czechoslovakia. Meets monthly except during July, August and September. Annual general meeting.

Deutsche Röntgengesellschaft
President, Professor Dr. med. Hanno Poppe, Radiologische Univ.-Klinik, Gossler Str. 10, 34 Göttingen, Germany.

Società Italiana di Radiologia Medica e di Medicina Nucleare
Secretary, Dr. Ettore Conte, Ospedale Mauriziano Torino, Italy. Meets annually.

Nederlandse Vereniging voor Radiologie
Secretary, Dr. C. B. A. J. Puijlaert, Prof. Dondersstraat 73, Tilburg, Netherlands.

Scandinavian Radiological Society
Secretary-General, Professor C. E. Unnérus, M.D., Hagalung-Tapiola, Havsvindsvägen 5 C., Finland.

Sociedad Española de Radiología y Electrología Médicas y de Medicina Nuclear
Secretary, Juan Gómez López, Villanueva, 11, Madrid 1. Meets every second Friday of each month, Oct. to June, inclusive, in Madrid.

Schweizerische Gesellschaft für Radiologie und Nuklearmedizin (Société Suisse de Radiologie et de Médecine Nucléaire)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

Asia

Indian Radiological Association
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

Indonesian Radiological Society
Secretary, Professor Sjahriar Rasad, Taman Tjut Mutiah I Diakarta, Indonesia

Iranian Radiological Society
Secretary, Dr. Issa Yaghmai, P.O. Box No. 14-1151, Teheran, Iran. The Society meets on the second Saturday of each month.

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ROENTGEN DIAGNOSIS

ABDOMEN

ASHBY, E. C., MOTT, T. J., and STARER, F. Severe gastrointestinal haemorrhage: haemangiomata demonstrated by selective visceral arteriography. *Brit. M. J.*, Dec. 21, 1968, *4*, 737–739. (From: Westminster Hospital, London S.W. 1, England.)

Conventional clinical methods often fail to show a cause for gastrointestinal hemorrhage. The failure rate has been of the order of 15 to 33 per cent in some large series. Gastrointestinal hemorrhage of obscure origin may be due to hemangiomata much more frequently than is recognized, since these are difficult to find at operation.

Two case histories are presented on patients hospitalized with severe gastrointestinal bleeding. In spite of exploratory laparotomy, the cause of bleeding was not determined in either. Selective superior mesenteric arteriography demonstrated an arteriovenous fistula in one and a small jejunal hemangioma in the other.

Gentry found 106 cases of alimentary hemangiomata in 1,400,000 Mayo Clinic case records, but almost half of these were discovered at autopsy. The stomach accounted for 12 per cent and the small intestine for 45 per cent. The diagnosis was rarely made preoperatively but might be suggested by the presence of cutaneous or mucosal hemangiomata, or by groups of phleboliths outside the pelvic area on plain roentgenograms. Bleeding could begin at any age, with the peak incidence at 20–50 years. The average length of history of intermittent bleeding was 12 years, but had been recorded to be as long as 40 years. Multiple lesions were twice as common as single. Males were affected twice as often as females—a reversal of the usual ratio in cutaneous hemangiomata.

Percutaneous selective visceral arteriography is found to have a high technical success rate with the celiac and superior mesenteric arteries and with the inferior mesenteric artery in other than elderly subjects. Caution is necessary when the circulation is slowed by shock or cardiac failure because of a risk of femoral artery thrombosis in those circumstances. During active bleeding, diagnosis depends on the recognition of contrast material escape from the vessel into the lumen of the bowel. It is suggested that pooling of contrast medium at the site of hemorrhage can be visualized if the bleeding rate is greater than 0.5 ml. per minute. When bleeding has ceased the source might be indicated by an abnormal vascular pattern due to a primary vascular abnormality, a tumor, or an inflammatory lesion.

It is debatable whether preoperative arteriography should be done routinely in cases of gastrointestinal hemorrhage of obscure origin. The added risks of arteriography must be weighed against the risks of an unnecessarily prolonged or fruitless operation. In cases where a previous laparotomy has not shown the cause of bleeding (or the extent of the lesion), or where the general condition of the patient would make a prolonged operation hazardous, or where superficial hemangiomata are found, the balance of risks would certainly seem to favor arteriography.—*David Morse, M.D.*

CREEDON, F. The adult pyloric mucosal diaphragm. *Brit. J. Surg.*, Nov., 1968, *55*, 818–822. (Address: The Surgical Registrar and Tutor, The Charitable Infirmary, Dublin, Ireland.)

The existence of an adult pyloric mucosal diaphragm was first noted by Albot, Renaux and Girard in 1946. Since then a total of 44 cases have been reported in the literature including 2 presented in this paper. The diaphragm consists of mucosa, submucosa and muscularis mucosae and is in almost all instances incomplete. The etiology is obscure although the occurrence of diaphragms in infants gives rise to the congenital theory.

Symptoms consist of vomiting (32 cases), epigastric pain (29 cases) and weight loss (18 cases).

There is no sex predominance and the peak age incidence is between 50 and 60 years.

A pyloric diaphragm has never been demonstrated roentgenographically, but may be suspected when there is pyloric obstruction without obvious cause. A prepyloric or antral diaphragm is occasionally visualized on barium studies as a thin linear filling defect. Associated gastric ulcer was found in 15 patients. Occasionally there is poststenotic dilatation of the duodenum.

Surgery provides relief of symptoms.

Two cases are reported and discussed.—*Herbert Helbig, M.D.*

HARVEY, A. J., and ROBERTSON, ANGUS. The use of an anal stimulator for barium enema examinations. *Australasian Radiol.*, Nov., 1968, *12*, 393–394. (Address: Dr. A. J. Harvey, Technical Officer, Repatriation General Hospital, Adelaide, So. Australia.)

The authors state that the use of an anal stimulator was initially developed for the more elderly patients who, as a normal aging process, have gradually lost their rectal control and sphincteric tone, but that they are now using the procedure for all barium enema examinations. They do not claim that it is foolproof, but they believe that they have significantly increased their percentage of "clean enemas."

The main complications would appear to be: (1) Electrical skin burns. So far this has not occurred but must remain a definite hazard. (2) Pain. Stimulation and contraction of the sphincters and pelvic floor muscles appear to cause an unusual but not

painful feeling. (3) Stimulation of the pudendal nerves and of the nervi erigentes. This has not been a problem so far, but the authors insist that a female insert the nozzle in female patients and remain throughout the examination. (4) Postexamination effects. No complications with regard to subsequent bladder or rectal evacuation have so far been recorded. (5) Rupture of the colon. So far this has not happened. (6) Tissue polarization. Electrical polarization of the tissues is most likely to occur when the stimulation is maintained over long periods, *i.e.*, for several months, for rectal and urinary incontinence. It is not considered to be a hazard during the short period of stimulation at barium enema examinations.—*Douglas S. Kellogg, M.D.*

Ritchie, G. W., Jackson, D. C., and Eaglesham, H. Percutaneous transhepatic cholangiography: experience with 54 cases. *Canad. M. A. J.*, Jan. 18, 1969, *100*, 110–116. (Address: Dr. G. W. Ritchie, Director, Department of Radiology, St. Boniface General Hospital, St. Boniface 6, Manitoba, Canada.)

The authors describe their experience with 54 cases of jaundice which was studied by percutaneous transhepatic cholangiography.

The indications for the procedure and the technique are described in detail.

In their series the examination was successful in 40 cases. Cannulization was unsuccessful in only 16 per cent of 43 patients with obstructive jaundice, but in 55 per cent of the 11 patients with hepatocellular disease. They feel that an unsuccessful examination is inconclusive, since extrahepatic biliary obstruction was present in 50 per cent of their failures.

Complications of bile peritonitis and internal hemorrhage are best avoided by restricting the study to the immediate preoperative period. None of the patients developed septicemia and there were no deaths attributable to the procedure.

The roentgenographic findings in choledocholithiasis with distal obstruction, carcinoma of the head of the pancreas, ampullary carcinoma, carcinoma of the body of the pancreas, carcinoma of the bile ducts, benign strictures, and metastatic lesions, are described in detail, with excellent illustrations.

A correct diagnosis was made in 39 out of the 40 successful cases.

The authors feel that the information provided by percutaneous transhepatic cholangiography will obviate the need for an unnecessarily difficult surgical exploration. Precious time can be saved in preoperative evaluation and at operation, with possible reduction in mortality and morbidity.—*James R. Knapp, M.D.*

Gynecology and Obstetrics

Fogarty, Thomas J., Wood, James A., Krippaehne, William W., and Dennis, Daniel L. Management of iliofemoral venous thrombosis in the antepartum state. *Surg., Gynec. & Obst.*, Mar., 1969, *128*, 546–550. (From: The University of Oregon Medical School Hospitals and Clinics, Portland, Ore.)

Iliofemoral thrombophlebitis or "milk leg" has remained a serious postpartum problem for the obstetrician. Recent reports suggest that there is a rising incidence of thrombophlebitis of the deep veins, not only in patients treated with estrogen or progestogen and in antepartum patients, but also in previously healthy young adults. The condition gives rise to an increased maternal and fetal mortality rate. Venographic studies have substantiated the fact that in some positions the fetus may completely occlude the venous outflow of the lower extremity. This occlusion is increased in the recumbent position.

Pulmonary emboli developed in 8 of 24 patients with this condition, and were responsible for the single death in the series.

The authors conclude that thrombectomy at the time of diagnosis is the treatment of choice.

Heparin is preferred to dicumarol as an anticoagulant because it has less effect on the fetus. Four of 5 venograms obtained from 2 to 10 months after cessation of heparin therapy demonstrated venous patency with normal valves.—*Arch H. Hall, M.D.*

Coucourde, F. L'importanza dell'esame radiologico del tubo digerente e delle vie urinarie nei tumori ginecologici. (The importance of the radiologic examination of the digestive and urinary tracts in gynecologic tumors.) *Ann. radiol. diag.*, 1968, *41*, 407–430. (From: Istituto di Radiologia e Terapia Fisica dell' Università di Pavia, Pavia, Italy.)

In order to evaluate the role of urography and of roentgenologic examinations of the gastrointestinal tract in patients affected by gynecologic conditions, the author has reviewed the data collected during the past 10 years in the Department of Radiology of the Medical School of Pavia.

These conclusions are presented: (1) roentgen studies of the gastrointestinal tract provide the radiologist with accurate information for the diagnosis of the various types of ovarian cysts; (2) intravenous urography permits the correct localization and diagnosis of paraovarian cysts and of multinodular fibromas of the uterus; (3) in patients with chronic pelvic inflammatory processes or with malignant neoplasms of the uterus, neither urography nor gastrointestinal tract examinations are of value. The only possible pathologic changes which can be demonstrated are the secondary ones involving either several loops of bowel and/or the ureters.

Numerous illustrations of the different roentgen findings accompany the article.—*A. F. Govoni, M.D.*

Nordin, B. E. C., Young, M. M., Bentley, B., Ormondroyd, P., and Sykes, J. Lumbar spine densitometry, methodology and results in relation to the menopause. *Clin. Radiol.*, Oct., 1968, *19*, 459–464. (From: The Medical Research Council, Mineral Metabolism Research Unit, General Infirmary, Leeds, England.)

A method of quantitative lumbar densitometry involving the simultaneous roentgenographic exposure of a patient and a normal lumbar spine segment mounted in saline is described.

The roentgenographic density of the vertebrae relative to the intervertebral disks is determined for the patient and a standard taken from a singly exposed film of both. A correction is made for vertebral body size and the results are expressed in mg. of bone ash per ml. of bone.

In premenopausal women, vertebral density ranges from 140 to 310 mg./ml. and the values are lower after menopause (130 to 240). A lower limit of vertebral density seems to be reached soon after menopause in normal women which does not decrease with further aging. Artificial menopause results in a rapid decrease but the ultimate level reached is similar.

Interference of overlying gas bubbles and obliquity of the spine must be avoided for technically satisfactory roentgenograms. The reproducibility of the method is ±6 per cent.—*John T. Underberg, M.D.*

Genitourinary System

Lytton, Bernard, Brooks, Marvin B., and Spencer, Richard P. Absorption of contrast material from the urinary tract during retrograde pyelography. *J. Urol.*, Dec., 1968, *100*, 779–782. (From: The Department of Surgery, Section of Urology and the Department of Radiology, Section of Nuclear Medicine, Yale University School of Medicine, New Haven, Conn.)

Allergic reactions to the intravenous injection of radiopaque medium for excretory urography are well documented. In this article the authors have attempted to evaluate the amount of absorption of a radiopaque medium after retrograde pyelography and the possibility of a systemic reaction therefrom.

Retrograde pyelography was performed in 10 adult patients using renografin labeled with I^{131}. The radioactive renografin was added to an equal volume of nonradioactive renografin to give an approximate concentration of 30 per cent, which provided satisfactory visualization for retrograde pyelography. The radiopaque medium was injected through a disposable ureteral catheter and the contrast material was left in place for 5 minutes after which time the renal pelvis was drained. Nonradioactive renografin was used for any additional pyelograms which were required. At the termination of the procedure the bladder was emptied. Blood samples were obtained prior to the injection and at intervals of 10, 20, 30 and 60 minutes following injection. In some cases blood samples were also taken at 2 and 24 hours. The radioactivity of the blood samples was determined in a Picker Spectroscaler III A counter. The total amount of contrast material absorbed was then calculated from the patient's estimated blood volume.

Eight of the 10 patients absorbed less than 1 per cent of the injected radioactive material. One patient absorbed 1.9 per cent and 1 patient absorbed 12.5 per cent.

The kidneys of 5 patients were normal and the remaining 5 had a variety of renal abnormalities, including 2 with hydronephrosis, 1 with chronic glomerulonephritis and 1 with a renal artery thrombosis. The maximum absorption occurred within 20 minutes after injection. Two of the patients who had significant quantities of radioactive material detected in the peripheral blood at the 24 hour interval had evidence of renal insufficiency. The 1 patient who had 12.5 per cent absorption of the radioactive medium showed a pyelogram with obvious pyelovenous backflow, but otherwise normal. Scanning of the thyroid gland for radioactive iodine in 1 patient showed no evidence of uptake at 6 and 24 hours, indicating that the radioactive I^{131} was not present in the circulation in its free form.

Previous studies of the absorption of radiopaque medium through the urinary epithelium, and this study, confirm the fact that a small amount of contrast material may be absorbed under normal conditions. In some circumstances where pyelovenous backflow occurs during retrograde pyelography, the amount of material absorbed is considerably increased above normal.

Clinical experience indicates that a serious hypersensitivity reaction is unlikely to occur during retrograde pyelography. However, the possibility cannot be completely ignored since some absorption of contrast material does occur, and since only small amounts may be required to produce a reaction in a susceptible individual.—*George W. Chamberlin, M.D.*

Cen, M., and Rosenbusch, G. Nierenangiographie mit Adrenalin (Möglichkeiten der Pharmakoangiographie). (Renal angiography with adrenalin; the possibilities of pharmacoangiography.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, Dec., 1968, *109*, 702–711. (Address: Priv.-Doz. Dr. M. Cen, Oberarzt, Klinische Anstalten der Rhein.-Westf. Techn. Hochschule, Abt. Radiologie, Goethestrasse 27/29, 51 Aachen, Germany.)

The use of adrenalin in conjunction with renal angiography is safe and improves the opacification of

tumoral vessels by causing constriction of the arteries in normal renal tissues as well as in most of the neighboring larger vessels.

A dose of 0.5 μg. per kg. body weight is injected by hand within 2–3 seconds when the catheter tip is at the level of the renal arteries. Injection at this level produces minimal vasoconstriction of more craniad arteries and no contraction of the posterior intercostal or lumbar arteries, while opacification of renal vessels is greater and lasts longer. If the catheter tip is above the celiac axis, the main branches of the celiac and superior mesenteric arteries will be reduced in caliber.

It is preferable to have the patient prone rather than supine because the former position permits less contrast material to flow towards the thoracic aorta; the superior mesenteric artery is better opacified in its entire length, and the intercostal arteries are not as well opacified.

The vasoconstriction is maximal about 20–30 seconds after the injection, whether made above the celiac axis or 1–2 cm. above the renal arteries.

In normal subjects there is no contrast material in the main stem after 20 minutes and there is no contraction of the main renal artery.

In hypertensive persons, weak contractions are seen in peripheral branches. In renal carcinoma, there is no or minimal contraction of tumoral vessels and heightened opacification of the involved area as well as the draining veins when the normal parenchyma is no longer opacified. Renal artery stenosis close to the aorta is more easily identified, but this method furnishes little information about more distally located stenotic vessels.—*J. Zausner, M.D.*

Staab, Edward V., Kelly, William D., and Loken, Merle K. Prognostic value of radioisotope renograms in kidney transplantation. *N.M. J. Nuclear Med.*, Mar., 1969, *10*, 133–135. (Address: Dr. Merle K. Loken, Nuclear Medicine Clinic, University of Minnesota Hospitals, Minneapolis, Minn. 55455.)

This report evaluates the usefulness of serial radioisotope renograms in predicting the rejection reaction following renal transplantation. Thirty-six patients who received either a live or cadaver transplant were studied. Renograms were obtained in the recovery room, 24 hours after surgery and daily for 1 week. Subsequent renographies were performed as dictated by the clinical course. Two parameters were used to describe the renogram numerically: the "time to peak" expressed in minutes; and a ratio of the height at 20 minutes divided by the height at the peak.

In 17 patients the transplants never functioned and the renogram was grossly abnormal in each of these instances. The remaining 19 patients had a clinical diagnosis of rejection reaction on 30 separate occasions. On 26 of these occasions the renogram correlated with the clinical impression. In 10 of the 26 instances the renogram correctly predicted the rejection reaction, in 13 it became abnormal at the same time the rejection was clinically apparent and it lagged behind in 2 instances. In the remaining case renograms were not obtained until after the rejection diagnosis was made.

On 4 occasions the renogram remained normal in the face of a diagnosis of rejection. All of these patients subsequently recovered. Sixteen renograms were abnormal in patients who had no other evidence of rejection. In each instance normal renograms were obtained shortly before and immediately after these abnormal patterns were seen.—*Howard West, M.D*

Mogg, Richard A. Congenital anomalies of the urethra. *Brit. J. Urol.*, Dec., 1968, *40*, 638–648. (Address: Consultant Urologist, United Cardiff Hospitals and Welsh Hospital Board, Cardiff, Wales.)

Congenital lesions of the urethra may produce severe bladder and ureteral dilatation. Associated renal damage is usually in direct proportion to the severity of the obstruction. Since micturition begins in the fetus in the third or fourth intrauterine month, a severe congenital obstruction can produce dilatation and irreparable damage which may be incompatible with life or cause death in the early neonatal period from renal insufficiency. Less severe obstructions, while possibly not life threatening, often result in significant morbidity.

The author reviews various congenital anomalies affecting the urethra as tabulated below:

(1) Anterior urethral stenosis and atresia
(2) Meatal stricture
(3) Anterior urethral diverticulum
(4) Duplication of the urethra
  (a) complete and
  (b) incomplete types
(5) Posterior urethral valves
(6) Urethral anomalies associated with anal atresia
  (a) imperforate anus with a perirenal fistula
  (b) atresia ani-urethralis and
  (c) atresia with rectovesical fistula
(7) Agenesis of musculature of the abdominal wall
(8) Tumors of the urethra

The embryology, clinical symptoms, roentgenologic or anatomic appearance, treatment and prognosis are briefly presented.—*Richard C. Pfister, M.D.*

Mitchell, J. P. Injuries to the urethra. *Brit. J. Urol.*, Dec., 1968, *40*, 649–670. (Address: Consultant Urologist, United Bristol Hospitals and Southmead General Hospital, Bristol, England.)

The author presents data on 60 cases of injury to the lower urinary tract, of which 43 were urethral

ruptures and the remainder involved the bladder. Combined injuries to the bladder and posterior urethra occurred in 18 per cent. Only 6 injuries involved the anterior urethra, while 37 posterior urethral ruptures were encountered. Two unusual cases involved the infrequently affected female urethra. In cases of fractured pelvis only 5 per cent had associated lower urinary tract damage which is attributed in the majority of cases to traffic accidents. Fractured pelvis resulting from crush injuries commonly leads to urethral damage in 15–25 per cent of patients.

"Complete" indicates transection of the urethra, with no trace of continuity between the 2 ends. In partial rupture, there is a full thickness tear of the wall of the urethra, but some mucosa remains bridging the gap. "Contusion" refers to any injury which is not a full thickness tear.

The triad of signs diagnostic of rupture of the urethra are: blood at the external meatus, inability to pass urine, and subsequently a distended bladder.

The diagnostic catheter is condemned in favor of clinical assessment because of the dangers of its use which are: risk of introducing infection; risk of adding further damage to the partially ruptured urethra; and, lastly, the serious risk of false diagnosis.

Urethrography's greatest value is in the anterior urethral injuries, as these are less frequently associated with multiple trauma. However, the patient in whom an urgent decision is required before he is due to go to surgery for his other injuries is also benefited by urethrography. If the urethrography is delayed until the second week, it is often impossible to introduce the contrast medium beyond the site of injury, which is obstructed by organizing blood clot. An S-bend deformity is found frequently in posterior urethral injuries resulting from displacement of the prostate. This indicates that the problem of stricture is as much a question of distortion as one of stenosis.

The principal complications of urethral rupture can be divided into those occurring in the early stages, which are mainly due to infection, and those occurring at the later stages, such as stricture with its sequelae, sexual impotence and urinary incontinence.—*Richard C. Pfister, M.D.*

Badenoch, Alec W. Traumatic stricture of the urethra. *Brit. J. Urol.*, Dec., 1968, *40*, 671–676. (From: St. Bartholomew's Hospital, London, E.C.1, England.)

The adult male urethra is a canal of variable length and caliber, but is usually 25–30 cm. long and has a diameter of 7 to 10 mm.

There are several regions in the course of the canal at which stricture commonly occurs. These are at the bladder neck, distal part of the prostatic or membranous portion, in the bulbous portion of the anterior urethra, at the peno-scrotal junction and at the fossa navicularis adjacent to the external meatus.

The author presents his experience of 69 cases with external traumatic strictures of the urethra. Of these, 34 per cent were intrapelvic urethral strictures resulting from external trauma to the bony pelvis, which is commonly fractured; the injury to the canal is indirect. The prostate is sheared off the membranous urethra near the triangular ligament or perineal membrane.

Bulbar strictures were the most common (55 per cent) and result from a direct type of external injury, usually straddle in nature, although impaction on any blunt object may result in stenosis of the bulbous urethra.

Peno-scrotal stricture was the least frequent.

Iatrogenic stricture following surgical intervention may occur anywhere but does so commonly at 3 sites. Stenosis of the bladder neck occasionally follows prostatectomy. Stricture at the peno-scrotal junction is usually due to passage of a large instrument. Meatal stenosis, or more often narrowing at the fossa navicularis, follows use of a red rubber indwelling catheter. This problem can be reduced by use of smaller catheters of plastic material

Many urethral stenoses will respond to periodic dilatations, while severe strictures require direct surgical repair.

Urethral false passages, perineal and suprapubic fistulae, urethral and bladder diverticula, urethral, bladder and renal stones, dilatation of upper tract and infection are complications of urethral stricture.

Roentgenologic examination is most important and should include excretory urography, and whenever possible a micturating urethrogram.—*Richard C. Pfister, M.D.*

Myers, George H., Jr., Lynn, Hugh B., and Kelalis, Panayotis P. Giant cyst of the utricle. *J. Urol.*, Mar., 1969, *101*, 369–373. (From: The Sections of Pediatric Surgery and Urology, Mayo Clinic and Mayo Foundation and the Mayo Graduate School of Medicine, Rochester, Minn.)

The authors report the case of an infant with hypospadias and incomplete testicular descent who also presented a giant cyst of the utricle.

The case is that of a 2 month old male infant with peno-scrotal hypospadias, bifid scrotum and bilateral undescended testes. On physical examination the patient was found to have a large mass extending from the low pelvis to the level of the umbilicus. Excretory urography showed normal upper collecting systems, but both ureters were deviated laterally around the soft tissue mass in the pelvis. A retrograde cystogram demonstrated an accessory sac-like structure arising from the posterior urethra. Endoscopy revealed absence of the veru montanum. To the left of the midline and arising posterior and proximal to the external sphincter, there was an orifice to a large diverticulum which was easily entered with the instrument.

Surgical exploration through a transverse supra-

pubic incision revealed a large fluid filled structure displacing the bladder anteriorly and to the right, so that the bladder was actually pushed out of the pelvis. Both ureters were seen to be displaced laterally. The cyst was dissected free down to its insertion into the urethra and then was excised. The exploration of the peritoneal cavity disclosed a right intra-abdominal testicle. This was brought into the scrotum and anchored. The left testicle was in the inguinal canal.

Subsequent endoscopy 6 months later showed a 2 mm. pocket where the utricle had been connected to the posterior urethra. The bladder appeared normal and a retrograde cystogram and urethrogram were normal, except for left vesical-ureteral reflux.

The large cyst which consisted of a pear-shaped sac measuring 6 by 3 by 3 cm. showed a wall of smooth muscle and was lined with transitional epithelium.

Microscopic sections through the neck of the cyst revealed many gland-like structures having the appearance of immature prostatic tissue.

The prostatic utricle is derived from the fused ends of the müllerian ducts and is the homologue of the female uterus and upper vagina. It varies in size and shape, with a length ranging from 8 to 10 mm. and a width of 1 to 6 mm. The utricle undergoes senile involution and usually does not produce clinical symptoms.

Müllerian duct cysts should be differentiated from an enlarged utricle, since the latter occurs most frequently during the first and second decades of life and is always associated with hypospadias and incomplete testicular descent. Furthermore, cysts of the utricle are usually easily excised in contrast to large müllerian duct cysts which are densely adherent to the posterior wall of the bladder, prostate and seminal vesicles.

The reported case is an unusual one with all features consistent with an enlarged utricle and concerns the youngest patient in whom this anomaly has ever been detected clinically.

The authors use 6 illustrations to demonstrate the clinical, surgical and roentgenographic pathologic changes.—*George W. Chamberlin, M.D.*

Reschke, H. Die Bedeutung der selektiven Nebennieren-Arteriographie für die Diagnostik des "Conn-Syndroms." (The significance of selective adrenal arteriography in the diagnosis of Conn's syndrome.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, Dec., 1968, *109*, 721–729. (Address: Oberarzt im Univ.-Strahleninstitut, Röntgeninstitut der Chirurgischen und Neurochirurgischen Universitätskliniken, 665 Homburg/Saar, Germany.)

Conn's syndrome is due to diffuse nodular hyperplasia of the adrenal cortex, which produces "primary hyperaldosteronism" with normo- and hypokalemic hypertensive forms.

Selective angiography is the best method for identification of the lesion and leads to fewer false positive diagnoses than percutaneous suprarenal venography or flush aortography with or without perirenal insufflation. The size or shape of a neoplastic area is not diagnostic nor can nodular hyperplastic changes be readily differentiated from normal adrenal glands or those with regressive alterations.

The left adrenal gland is more frequently involved than the right. The left adrenal gland also varies more commonly in size and structure than the right.

In the author's series, adrenal adenomas were found in 20 per cent of hypertensive patients and in 2 per cent of normotensive subjects. Glucose intolerance occurred in 50 per cent of patients with primary aldosteronism and the diabetic metabolism remained essentially unchanged following adrenalectomy.

Angiography was successful in 90 per cent and only partially successful in 70 per cent in patients studied for primary aldosteronism.—*J. Zausner, M.D.*

Skeletal System

Smith, Taylor K., Gregersen, Gary S., and Samilson, Robert L. Orthopaedic problems associated with tuberous sclerosis. *J. Bone & Joint Surg.*, Jan., 1969, *51A*, 97–102. (From: The University of California, San Francisco Medical Center, Department of Orthopaedic Surgery, San Francisco, Calif. 94122.)

Tuberous sclerosis has been classified as a phakomatosis along with neurofibromatosis and the various angiomatoses such as Sturge-Weber-Dimitri, Lindau-von Hippel and retinocerebellar angiomatosis. All are congenital conditions in which obvious pathologic birthmarks on the skin, retina and viscera are seen.

Tuberous sclerosis presents in its classic form with symptoms of mental retardation, adenoma sebaceum and epilepsy. In addition to the classic triad, patients with tuberous sclerosis may also have other neurocutaneous, visceral or osseous abnormalities.

In reviewing the records of more than 3,400 patients at Sonoma State Hospital, 32 (17 female and 15 male patients) had the classic triad of tuberous sclerosis. They ranged from 5 to 37 years of age and all were Caucasians. All were examined for orthopedic abnormalities and their roentgenograms and charts were reviewed.

Twenty of these patients were ambulatory, 1 was confined to a wheel chair and the remaining 11 required total bed care. Seven were found to have no orthopedic problems. Three had minimal abnormalities (planovalgus feet or external tibial torsion). Twenty-two patients had significant orthopedic abnormalities which interfered with activities or re-

quired orthopedic treatment. There were 16 fractures and 3 dislocations in the past history of these patients but none were through bone lesions and all were associated with a history of significant trauma. All of the cases confined to bed had flexion adduction contractures of the hips and shoulders and flexion contractures of the knees and elbows. Their deformities were typical of bedridden spastic patients. Deformities in the ambulatory patients were typical of mild spasticity with most of the patients being toe walkers. Two patients had a significant degree of scoliosis and 2 had bilateral untreated talipes equinovarus deformities.

Tuberous sclerosis has been implicated as a congenital cause of cerebral palsy and 19 of the 32 patients in this series showed some degree of cerebral palsy, often with various fixed joint contractures. The majority of the orthopedic problems were felt to be due to the neurologic elements of the disease and the treatment rendered was the same as for comparable problems stemming from other causes.

The authors also review briefly the history and the roentgenographic findings associated with this disease.—*Victor J. DiOrio, M.D.*

CHUNG, STANLEY M. K., and RALSTON, EDGAR L. Necrosis of the femoral head associated with sickle-cell anemia and its genetic variants: a review of the literature and study of thirteen cases. *J. Bone & Joint Surg.*, Jan., 1969, *51A*, 33–58. (From: The Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia, Pa. 19104.)

The association of necrosis of the femoral head with both typical and atypical sickle-cell disease has been recognized for many years. The authors give a concise, up to date review of the pertinent genetic, chemical and clinical information on this subject.

Hemoglobin synthesis is under strict genetic control, the primary function of the genes in question being the regulation of the amino acid sequence in the polypeptide chains comprising the globin fraction. Disturbances in this amino acid sequence result in variations from the normal adult hemoglobin. Diagnosis is based upon hemoglobin electrophoresis.

The more severe clinical picture of classic sickle-cell disease (homozygous SS state) is discussed and compared with the milder variant forms of sickle disease (the S gene in combination with another mutant hemoglobin gene). Avascular necrosis of the femoral head in the former is less common (4–12 per cent) than in the variant sickle-cell states. This is particularly true in sickle-cell hemoglobin C disease, where the reported incidence varies from 20–68 per cent. However, other areas of bone infarction and generalized bone changes due to erythroid hyperplasia are more frequent in the homozygous state. These other bone changes, which have frequently been described in association with sickle-cell disease, are briefly summarized.

Sickle-cell disease is known to occur in Caucasian Mediterranean groups (sickle-cell thalassemia) as well as in the Negro. A patient in this study was a white Greek female with classic SS disease.

Thirteen cases of known homozygous or heterozygous sickle-cell disease with femoral head necrosis are summarized and illustrated with roentgenographic reproductions. Patients with the homozygous state, as expected, exhibited other bone changes more frequently than those with variant states.

The authors attempted to group their patients by roentgen and clinical findings.

Group I included individuals with a "Legg-Perthes" type of involvement of the capital epiphysis or femoral head. Features which aided in differentiating hip involvement due to sickle-cell disease from idiopathic or Legg-Perthes disease were a generally later onset of clinical symptoms, sparing of the metaphysis in sickle-cell disease, and race (Legg-Perthes disease is rare in Negroes). Patients treated in this group displayed a predictable course with eventual replacement of the necrotic bone.

Group II featured patients with localized necrosis of the femoral head typical of osteochondritis dissecans. It is suggested that patients in either of these two groups will improve with conservative management.

Group III, usually older individuals, had hip deformities which did not improve with conservative measures.

Avascular necrosis of the femoral head secondary to sickle-cell disease may be more common than realized. Stress is placed on obtaining hemoglobin electrophoresis on all Mediterranean and Negro patients with hip disease, especially idiopathic avascular necrosis.—*Charles C. Nicolette, M.D.*

DUMANIAN, ARA V., and KELIKIAN, H. Vascular complications of orthopaedic surgery. *J. Bone & Joint Surg.*, Jan., 1969, *51A*, 103–108. (Address: Dr. Ara V. Dumanian, St. Catherine Hospital, 4312 Fir Street, East Chicago, Ind. 46312.)

Operative damage to vascular structures may occur whenever a surgical procedure is performed in close proximity to major arteries and veins. The authors report 3 cases with such vascular complications.

The first patient is a 37 year old woman who had intervertebral disk surgery 4 years before admission. Three years later she was re-operated on because of persisting symptoms. Another disk was taken out and a spinal fusion was performed. During the second operation she went into shock while the wound was being closed. She was treated with blood transfusions and her pressure stabilized. After surgery she became weak with dyspnea on mild exertion. She also noted swelling of both legs and feet. The swelling was worse on the right side. Physical exami-

nation revealed venous engorgement over the right lower quadrant of the abdomen and costal margin. The right femoral pulse was weak and the right pedal pulse could not be felt. A pulsatile abdominal mass was palpable over the right lower quadrant over which a thrill could easily be felt. A chest roentgenogram revealed generalized cardiac enlargement. Angiography showed a large fistula between the right common iliac artery and vein. The fistula was closed and a dacron graft used to establish arterial continuity. The patient made an uneventful recovery.

The second patient is a 15 year old girl who required medial meniscectomy following a knee injury during a gymnasium class. When the synovial membrane was incised, a large quantity of bloody fluid under pressure escaped from the joint cavity. A medial meniscectomy was performed as a large tear in the flat posterior portion of the medial cartilage was encountered. Three days after surgery the right leg and foot became markedly swollen and pedal pulses could not be felt. She was initially treated with heparin and dicumarol with a diagnosis of acute thrombophlebitis. The swelling of the right foot and leg decreased. Her knee continued to hurt and there was marked swelling posteriorly. There was a pansystolic bruit over the bulge in the posterior portion. Arteriography was performed using the Seldinger technique. Arteriograms confirmed the diagnosis of traumatic aneurysm of the popliteal artery. This was resected and a vein graft utilized to establish continuity.

The third patient is a 16 year old boy who was seen with a huge mass in his left groin 2 years following pinning of a slipped capital femoral epiphysis. There was a very large mass over the left upper thigh, left groin and left lower quadrant of the abdomen. The left lower extremity was swollen. The mass pulsated on deep palpation and a large pansystolic bruit was heard over this mass. Arteriography confirmed the diagnosis of traumatic aneurysm of the left femoral artery. At surgery one of the hip pins was found extending into the cavity of the large aneurysmal mass.

The conclusion is reached that delay in diagnosis of these entities results in increased morbidity and greater difficulty in surgical repair.—*David Morse, M.D.*

Pearlman, Carl K., and Bors, Ernest. Congenital absence of the lumbosacral spine. *J. Urol.*, Mar., 1969, *101*, 374–378. (From: The Urology Division, Orange County Medical Center; the Spinal Cord Injury Service, Long Beach Veterans Administration Hospital; and the Department of Surgery, University of California, Los Angeles, Calif.)

This is a case report of a young adult male with congenital absence of the lumbar spine. The literature includes only 13 previously reported cases.

The patient was first seen by the authors at the age of 8 years, at which time he had complete urinary incontinence and fecal impaction. Roentgenographic examination showed a normal number of thoracic vertebrae, but an absence of the lumbar spine and a fused sacrum. Good renal function was noted on excretory urography.

The problem with this patient was control of the urinary incontinence and proper bowel function. Following a suprapubic cystostomy he continued to have leakage around the urethra. In order to correct this a sigmoidocystoplasty was done and the vesical neck was closed. A previous right colostomy had been done.

The case herein reported shows that suprapubic cystostomy is not a satisfactory procedure in a patient who has a lower motor neuron lesion. A urethral catheter is preferable and should be changed frequently. In this particular instance, urinary incontinence was eventually solved by surgical closure of the vesical neck and a colosigmoidostomy.—*George W. Chamberlin, M.D.*

Jones, Frank E., Soule, Edward H., and Coventry, Mark B. Fibrous xanthoma of synovium (giant-cell tumor of tendon sheath, pigmented nodular synovitis). *J. Bone & Joint Surg.*, Jan., 1969, *51A*, 76–86. (Address: Dr. Frank E. Jones, 200 First Street, S.W., Rochester, Minn. 55901.)

One-hundred and seventeen lesions in 118 patients with fibrous xanthoma of the synovium were studied clinicopathologically. Fibrous xanthoma is the second most common tumor of the hand; it is not common in other locations.

Roentgenograms were obtained in 91 patients. The abnormal findings were seen in 74 patients and consisted of soft tissue masses in 54, evidence of degenerative joint disease in the joint from which the xanthoma arose or in the joint nearest to it in 46, and erosions of bone adjacent to the lesion in 11 instances.

The authors believe that the lesion is caused by a proliferation and metaplasia of synovial histiocytes.—*Robert Dormire, M.D.*

Blood and Lymph System

Wendel, Richard G., Evans, Arthur T., and Wiot, Jerome F. A new technique for inferior venacavography. *J. Urol.*, Nov., 1968, *100*, 705–708. (From: The Departments of Urology and Radiology, University of Cincinnati Medical Center, Cincinnati, Ohio.)

Various methods of demonstrating the inferior vena cava have been attempted with many revisions over a period of years since dos Santos first demonstrated the feasibility of this procedure.

The authors have found success by the use of an Ödman-Leden red catheter with 5 precisely placed

and precisely sized holes placed along the catheter. By the Seldinger technique, the catheter is placed in the inferior vena cava with the tip at the level of the first lumbar vertebra. Injection of 30 cc. of 75 per cent hypaque at 98°F. was then made through the catheter at 275 pounds per square inch pressure. Concomitantly with the injection, the patient performs the Valsalva maneuver in full inspiration, and multiple serial roentgenograms are procured every second for 6 seconds by means of a rapid cassette changer.

This technique produces satisfactory demonstration of the vena cava. It eliminates the need for applying tourniquets to the thighs and does not require any compression devices over the upper abdomen. The procedure can be performed in the recumbent position and streaming or layering of the radiopaque material has not been a factor in the evaluation of the roentgenograms.

The authors stress that patient cooperation is essential for proper accomplishment of the Valsalva maneuver. Carelessness in the placement of the catheter or the size of the side hole diameters, the viscosity of the medium or the length of the catheter may affect the distribution of the contrast medium. The pressure injector and the rapid cassette changer are essential factors to proper technique.—*George W. Chamberlin, M.D.*

Shuford, W. H., Sybers, R. G., and Weens, H. S. Problems in the aortographic diagnosis of dissecting aneurysm of the aorta. *New England J. Med.*, Jan. 30, 1969, *280*, 225–231. (From: The Departments of Radiology, Emory University School of Medicine and Grady Memorial Hospital, Atlanta, Ga. 30303.)

Recent advances in the surgical treatment of dissecting aneurysm of the aorta have made precise evaluation of this disorder extremely important. The use of catheter aortography in the study of aortic dissection has greatly enhanced the quality of diagnostic examinations, in comparison with other techniques.

The authors reviewed 44 cases suspected of having dissecting aneurysms which were studied by catheter aortography. Findings of dissection were clearly present in 23, and in 11 the aortographic findings were considered to be negative.

In the remaining 10 cases unusual problems in diagnosis were encountered. In 2 patients with aortic dissection in whom the injection of contrast medium into the ascending aorta resulted in uniform filling of both channels, the presence of 2 channels was clearly established by catheter withdrawal and selective injection into the descending aorta. Multiple projections may be necessary also for localized opacification of a false channel, when the findings in the standard projections are questionable. A false channel of dissecting aneurysm was simulated by layering a contrast medium along the posterior wall of the descending aorta in a case of aortic insufficiency. The presence of abnormal to-and-fro pulsations together with filling of the intercostal arteries was evidence that the catheter was not in a false channel.

The most consistent aortographic finding has been compression of the true lumen by the false channel with irregularity of the affected side of the contrast stream and an increase in the extraluminal soft tissue thickness of the involved portion of the aorta. The presence of a narrowing of the true lumen on early roentgenographic studies with variable degrees of opacification of the false channel on later roentgenograms is also diagnostic. Occasional ulcer-like projections of contrast material from the true lumen may identify the site of intimal tear; a differential contrast density of the true lumen as compared with false channel is also typical. When the true lumen is narrowed with equal opacification of the false channel and true lumen, the diagnosis is dependent upon visualization of the dissected inner wall, which may appear as a radiolucent septum.

Abnormal thickening of the aortic wall in the absence of compression of the true lumen remains an uncertain sign of aortic dissection and other conditions; primarily, atherosclerosis, aortitis, and aneurysm with laminated thrombus, may produce this appearance. Extrinsically a mediastinal hematoma or tumor contiguous to the aorta may likewise be misleading.

The authors feel that the intravenous angiocardiographic method is suboptimal and catheter aortography should be used whenever feasible. The inadvertent positioning of a catheter within a false channel can be recognized by the use of small test injections.—*James R. Knapp, M.D.*

Cossette, Robert, Davignon, Andre, and Stanley, Paul. Ruptured aortic aneurysm in a $3\frac{1}{2}$ year-old child with coarctation of the aorta. *Canad. M. A. J.*, Feb. 1, 1969, *100*, 257–261. (Address: Dr. Paul Stanley, Hôpital Ste-Justine, 3175 Chemin Ste-Catherine, Montreal 26, Quebec, Canada.)

The authors report a case of ruptured pseudoaneurysm of the thoracic aorta associated with coarctation in a $3\frac{1}{2}$ year old child. Only 10 cases have been reported in the literature as a complication of coarctation in children under 9. The pathology usually could be attributed to: (a) cystic medial necrosis; (b) mycotic aneurysm; and (c) syphilis.

The patient reported, when diagnosed as coarctation, was 3 years of age. Chest roentgenograms showed slight cardiomegaly with left ventricular hypertrophy. The descending aorta was dilated.

Five months after angiography, the patient developed an upper respiratory tract infection. A week after the onset of the upper respiratory tract infection, the patient complained of chest pain, dyspnea

followed by hematemesis and hemoptysis. Chest roentgenograms showed a large posterior mediastinal mass in the superior mediastinum, displacing the trachea anteriorly.

Emergency surgery revealed a false aneurysm of the aorta beneath the coarctation on the anterior aspect of the aorta.

Bacteriologic culture demonstrated coccobacillus of the Moraxella type.

The patient was grafted and remains well with no unusual postoperative complications.—*Gonzalo Chua, M.D.*

General

Bateson, Eric M. Radiological observation on an alveolar soft-part sarcoma complicated by trauma and myositis ossificans. *Clin. Radiol.*, Oct., 1968, *19*, 389–393. (From: The Department of Radiology, University Hospital, Mona Kingston 7, Jamaica, West Indies.)

The alveolar soft-part sarcoma is a rare malignant tumor, recently identified, that has its origin from primitive nerve cells and shows histologic resemblance to chemodectoma. It is associated with the skeletal muscle and therefore usually seen in the extremities. It is often preceded by a history of trauma, is more frequent in females and tends to recur if locally excised. Metastases to the lungs frequently occur.

The present case was seen in a 17 year old Negro Jamaican who complained of pain and swelling in his thigh following trauma during a football game. Roentgenograms showed subperiosteal calcification that progressed to an extensive area of ectopic bone characteristic of myositis ossificans. Arteriography showed an irregular pattern of vessels and tumor stain thought by the authors to be similar to that of tumors of the chemoreceptor system.

Four months following dissection and local resection of the tumor which had extended to the groin, the patient developed a nodule at the healed operative site and hemoptysis. A chest roentgenogram revealed multiple oval metastases. He was lost to follow-up.—*John T. Underberg, M.D.*

Khajavi, Abol. Guinea worm calcification: a report of 83 cases. *Clin. Radiol.*, Oct., 1968, *19*, 433–435. (From: The Department of Radiology, Namazee Hospital, Pahlavi University, Shiraz, Iran.)

Soft tissue calcifications of the dead female guinea worm (*Dracunculus medinensis*) are frequently seen on roentgenograms in Africa and Asia. The roentgenograms of 83 patients seen at Namazee Hospital, Shiraz, Iran were reviewed.

Young worms, discharged from the female uterus, emerge from the host's skin and enter the water to be eaten by freshwater crustacean cyclops. The larvae in the cyclops penetrate the host's intestinal wall and migrate, usually to the retroperitoneal area, to mature in a year. After fertilization the males die and the gravid females migrate to the host's skin to be discharged through an ulcer.

The adult female worm is 75 to 120 cm. long. The calcified dead female worms are seen in the soft tissues of the extremities, chest, abdominal wall and perineum. Characteristically, the calcifications are long, spiral and segmental.

Interestingly, 15 of the 83 patients presented malignant disease in organs near the calcifications.—*John T. Underberg, M.D.*

Radiation Therapy

Gilmore, Shirley Ann. Alterations in blood vessels in x-irradiated spinal cords of young rats. *Anat. Rec.*, Jan., 1969, *163*, 89–99. (From: The Department of Anatomy, University of Arkansas Medical Center, Little Rock, Ark.)

Thirty-two litters of 3 day old Holtzman rats were used in this study. One hundred and thirty-five were irradiated and 59 used as a control group. A 5 mm. length of body over the spinal cord was irradiated with a single total dose of 2,000 r or 4,000 r of soft x rays from a Philips Contact Therapy Apparatus. The factors were: 50 kvp.; 2 ma.; 2.4 mm. Al filter; half-value layer 0.16 mm. Al; target-skin distance 8 cm.; and a dose rate of 722 r/min. The rats were sacrificed 1–27 days later.

There were loss of neuroglia and damage to the vasculature in the irradiated area. The animals receiving 2,000 r demonstrated transient changes which were reversible with delayed myelinogenesis. The more severe and apparently irreversible changes occurred with 4,000 r. Petechiae and perivascular globules in the 4,000 r group indicated a type of damage leading to ischemia.

The alkaline phosphatase staining technique in this experiment showed decreased alkaline phosphatase activity in the neutrophils. This change preceded any constant alteration in vascular alkaline phosphatase.

The results were felt to support the hypothesis that the vasculature is affected by the amount of radiation, and that the spinal cord changes are in part related to the severity of vascular alterations.—*Raymond W. Gize, M.D.*

Juliani, G., Piccotti, F., and Cirillo, R. Radioterapia e fenomeni immunitari nell'evoluzione del tumore di Ehrlich. (Radiotherapy and immunizing phenomena in the evolution of Ehrlich's tumor.) *Radiol. med.*, 1968, *54*, 556–573. (Address: Dott. Prof. Giovanni Juliani, Corso Massimo d'Azeglio, 100, Torino, Italy.)

The authors have conducted a series of experi-

ments on "Swiss" albino rats in order to study quantitatively the immunologic response of the host during the evolution of Ehrlich's tumor. Its variations were induced by radiotherapy, by vaccination with irradiated cells, and by the association of surgical removal of the lesion with vaccination with irradiated cells.

On the basis of these experiments the following conclusions are presented: (1) during the evolution of Ehrlich's tumor the host acquires a certain degree of resistance which, however, is not sufficient to modify the growth of the tumor itself; (2) the immunity which is acquired either spontaneously, or after radiotherapy, or by vaccination is relatively limited; (3) the resistance acquired by the animal after surgical removal of the tumor is not as significant as that observed in animals treated by radiotherapy, or by vaccination with irradiated cells; (4) the association of surgical removal of the tumor and vaccination produces a degree of immunity similar to the one induced by radiotherapy alone; and (5) the degree of immunologic reactions is moderate, and their contribution to the process of recovery is rather limited.—*A. F. Govoni, M.D.*

RADIOISOTOPES

Sephton, R. G., and Morley, J. Barrie. The two roles of the scan in the diagnosis of cerebral tumours. *Australasian Radiol.*, Nov., 1968, *12*, 328–343. (From: The Physics Department, Cancer Institute, Melbourne, Australia.)

A number of case reports are presented and it is stated that cephaloscans are potentially very sensitive for detection of supratentorial brain tumors and can detect some lesions which were undetectable by other means. The authors discuss experiences with cerebral tumors that fall in the latter category.

One conclusion is that scanning techniques frequently provide the earliest confirmation of the presence of a lesion; however, it is indicated that scanning is not a substitute for neuroradiology, but rather a complement.—*Abbas M. Rejali, M.D.*

Tefft, Melvin. Radioisotopes in malignancies in children: use in the study of involvement by primary and metastatic processes in brain and liver. *J.A.M.A.*, Mar. 10, 1969, *207*, 1853–1858. (Address: 300 Longwood Avenue, Boston, Mass. 02115.)

The author has summarized his experience with 1,500 cephaloscans and 800 hepatoscans of children. The material and method of scanning are described in detail.

The brain lesions were divided into subtentorial and supratentorial neoplasms. Of the subtentorial neoplasms, approximately 90 per cent low grade cerebellar astrocytomas and 45 per cent medulloblastomas showed positive scans. Of the supratentorial neoplasms, 85 to 90 per cent Grade 3–4 (highly malignant) gliomas and 15 to 20 per cent Grade 1–2 gliomas, and 65 per cent optic gliomas had positive scans. Also, 30 per cent of those patients with symptoms or signs of brain infiltration in acute leukemia revealed positive scans.

Approximately 85 per cent of the patients with metastasis to the liver demonstrated space occupying lesions, but all primary neoplasms of the liver (hepatoma) were demonstrated by scanning before laparotomy.

Scanning of the liver was used in all patients with abdominal masses and was very useful in both directing the plan of radiation therapy and in follow-up studies.—*Abbas M. Rejali, M.D.*

De Roo, M. J. K., Goris, M., Cosemans, J., Gyselen, A., Billiet, L., and Van Der Schueren, G. Computerized dynamic scintigraphy of the lungs. *J. belge de radiol.*, 1968, *51*, 338–347. (Address: Dr. M. J. K. De Roo, Academisch Ziekenhuis St-Rafael, Leuven, Belgium.)

This article describes a method for exploration of the regional lung function (perfusion and ventilation) using Xe^{133} and an Anger camera.

With the technique described, one can obtain not only qualitative and quantitative views of the distribution of xenon 133 within the lung but also a quantitative recording of tracer changes to permit a more thorough investigation of the regional pulmonary function.—*Abbas M. Rejali, M.D.*

Tori, G., Marabini, A., Cabassa, N., Giaretta, V., Tognetti, G. P., Tison, V., and Mazzanti, G. L. La scintigrafia con radiostronzio nell'osteodistrofia di Paget. (Scintigraphy with radiostrontium in the osteodystrophy of Paget.) *Radiobiologia, radioterapia e fisica medica*, 1968, *23*, 237–268. (From: Istituto di Medicina Nucleare dell'Università di Bologna and Istituto di Radioterapia dell' Ospedale Civile di Verona, Verona, Italy.)

The authors have conducted a series of studies with strontium 87m and strontium 85 in 7 cases of Paget's disease. Analyzed with bone scanning were the pathologic changes in the various segments of the skeletal system involved by the process.

The following conclusions are presented: (1) photoscanning of a Paget bone shows areas of high concentration of the radioisotope. The degree of concentration is higher than in other pathologic processes involving the skeletal system; (2) there are areas which are "silent," where no uptake of the radioisotope occurs, probably because of the stage

of evolution of the pathologic process; (3) scintiscanning cannot provide definite elements of diagnostic importance which would permit the correct diagnosis of Paget's disease; (4) however, this procedure can provide more accurate information on the stages of evolution of the disease.—*A. F. Govoni, M.D.*

Edwards, C. Lowell, and Hayes, R. L. Tumor scanning with ^{67}Ga citrate. *N. M. J. Nuclear Med.*, Feb., 1969, *10*, 103–105. (From: Oak Ridge Associated Universities, Oak Ridge, Tenn.)

Carrier free gallium 67 was used by the authors as a tumor scanning agent in 2 patients. One patient had Hodgkin's disease involving the lymph nodes in the neck region which took up sufficient gallium 67 to permit excellent scan images to be obtained. The second patient had a poorly differentiated thyroid carcinoma with known pulmonary metastases. The scan of the thorax following isotope administration showed significant uptake of the radioisotope in areas of metastatic involvement.

The authors state that further study, both in patients and in animals, is required to fully evaluate the efficacy of gallium 67 as a tumor scanning agent. —*Merle K. Loken, M.D.*

Negus, D., Pinto, D. J., Le Quesne, L. P., Brown, N., and Chapman, M. ^{125}I-labelled fibrinogen in the diagnosis of deep-vein thrombosis and its correlation with phlebography. *Brit. J. Surg.*, Nov., 1968, *55*, 835–839. (From: The Department of Surgery, St. Thomas's Hospital, London, England.)

I^{125} labeled human fibrinogen was injected intravenously between 1 and 3 hours after operation in 93 patients. Twelve hours later, the level of radioactivity was measured over the heart and at selected points on the legs. The measurements were repeated daily for 10 to 14 days following operation. The measurements were made using a portable scintillation counting system with the patient lying supine in his bed in the ward with the legs elevated 10° above the horizontal in order to avoid venous pooling.

Sixty-one patients showed no significant variation in percentage uptake made at the selected points on the leg from groin to ankle. In 32 patients, there was a difference of percentage uptake of 15 or more between adjacent points on the leg. In all patients this occurred at points over the calf, and in 1 patient there was also an increase over the mid-thigh of the same limb. Only 6 of these patients developed any signs compatible with deep-vein thrombosis. Phlebography was performed in 26 limbs of 19 patients from the elevated uptake group. In 24 limbs of the 18 patients in which there was an abnormal percentage uptake, a thrombus was demonstrated on phlebography. In 2 limbs of the other patients, a thrombus was not demonstrated. In the 29 limbs of 21 patients with no elevated percentage uptake, no thrombus was detected at phlebography.

The results demonstrate the reliability of the I^{125} fibrinogen method of detecting thrombosis in the deep veins of the leg, whether or not physical signs are present. Thrombosis was never diagnosed either clinically or phlebographically without an accompanying rise in the I^{125} fibrinogen radioactivity in the affected area.

No untoward reaction was observed in the series of 93 patients nor have any been reported in the literature.

The techniques of phlebography and the I^{125} labeled for fibrinogen procedure are described in detail. Possible confusing situations such as healing wounds on the legs are discussed.

I^{125} fibrinogen uptake is a simple method of detecting and monitoring deep vein thromboses.—*William T. Mc Laughlin, M.D.*

Murray, Shirley, and Wood, D. E. Myeloscintigrams in the assessment of lumboperitoneal shunts. *Canad. M. A. J.*, Feb. 8, 1969, *100*, 277–280. (Address: Dr. Shirley Murray, Toronto General Hospital, 101 College Street, Toronto 2, Ontario, Canada.)

The authors have used either iodine 131 serum albumin (100 microcuries) or technetium 99m albumin (1 millicurie) administered into the subarachnoid space for evaluation of lumboperitoneal shunts.

They employed either a point count technique or the scanning method to study the patency of these shunts. They found that the results of a point count technique, which was used in 6 patients, were difficult to interpret. On the other hand, the detail of the scans was sufficient to permit unequivocal determinations to be made in 4 patients, only 1 of whom showed a patent shunt.—*Merle K. Loken, M.D.*

Lieberman, Lionel W., Beierwaltes, William H., Varma, Vijay M., Weinhold, Paul, and Ling, Ronald. Labeled dopamine concentration in human adrenal medulla and in neuroblastoma. *N. M. J. Nuclear Med.*, Feb., 1969, *10*, 93–97. (From: The University Hospital, University of Michigan Medical Center, Ann Arbor, Mich. 48104.)

The authors have used carbon 14 labeled 3,4-dihydroxyphenylethylamine (dopamine) in studies of the human adrenal medulla and in patients with neuroblastoma. They found that the relative concentration of dopamine in the adrenal medulla is greater than the concentration of iodine 131 in thyroid metastases. This finding suggests that dopa-

mine may be useful in the detection of tumors involving the endocrine glands. The authors found a greater concentration of dopamine in human neuroblastoma than in the adrenal gland, but no significant concentration of this agent in either a primary hepatoma or neurolemmoma.

Preliminary attempts by the authors to incorporate a gamma emitter (radioactive iodine) into precursors of dopamine have been encouraging. If this can be successfully accomplished, a new addition to the armamentarium of tumor scanning agents will be available in the practice of nuclear medicine.—*Merle K. Loken, M.D.*

MISCELLANEOUS

MARCOVE, RALPH C., and MILLER, THEODORE R. Treatment of primary and metastatic bone tumors by cryosurgery. *J.A.M.A.*, Mar. 10, 1969, *207*, 1890–1894. (Address: Dr. Ralph C. Marcove, 517 E. 71st Street, New York, N. Y. 10021.)

The authors record their experience in the treatment of both primary and metastatic bone disease by two different cryosurgical techniques. The first method utilizes a double lumen probe which is applied to the lesion until the entire area is completely frozen. The second method is useful in large cystic lesions which lend themselves to curettement. A stainless steel funnel is sealed into the cavity with gelatin sponge following curettage. The cavity and funnel are then filled with liquid nitrogen and the entire area is frozen.

Fifty patients were treated a total of 57 times with these techniques. There were 7 recurrences and cryosurgery was repeated in each instance. All except 1 reported pain relief and remained pain free, excluding those cases where recurrences developed. Skin necrosis occurred in 6 patients and subsequent infection developed in 2. There were 4 postoperative fractures reported and transient nerve palsies were seen in 4.

The authors feel that freezing is indicated in locally destructive processes where wide excision or high dose radiation therapy is the alternative. They do not recommend it, however, in highly malignant localized primary bone tumors where treatment must be dependable and rapid to prevent distant metastases.—*Howard West, M.D.*

CHEMOTHERAPY

REYNOLDS, RALPH D., SIMERVILLE, JAMES J., O'HARA, DAVID D., HART, JOSEPH B., and PARKINSON, JOHN E. Hemorrhagic cystitis due to cyclophosphamide. *J. Urol.*, Jan., 1969, *101*, 45–47. (From: The Departments of Medicine and Surgery, David Grant United States Air Force Hospital, Travis Air Force Base, Calif.)

This is a case report concerning a 15 year old female with Hodgkin's disease of 5 years' duration. The patient had received 100 mg. of cytoxan orally daily for 4 years.

On admission to the hospital, there was gross hematuria. The platelet count was 20,000 and the blood urea nitrogen 41 mg. per cent. An excretory urogram showed that both ureters were dilated and there was blood in the excretory passages. A large amount of blood was evacuated from the urinary bladder and bleeding was noted from both ureteral orifices during cystoscopy. Biopsy of the bladder mucosa showed diffuse inflammation and edema. Cytoxan was discontinued and multiple transfusions were given. In spite of persistent thrombocytopenia, the hematuria disappeared. The patient, however, died subsequently of a yeast meningitis.

The severe hemorrhagic cystitis is considered to be a function of the concentration of the drug in the urinary tract and the duration of its contact with the bladder epithelium. This syndrome may begin suddenly and persist for a variable length of time, but it is potentially self-limited. It is best prevented by instructing patients to ingest large quantities of fluids and to void frequently. Early detection is important and the cause of the disease should be easily determined by cystoscopic examination. In the more advanced cases, the healing bladder will have a smaller capacity due to fibrosis.

The authors illustrate the histopathologic changes in the bladder.—*George W. Chamberlin, M.D.*

MÖBIUS, G., PÜSCHEL, W., and SCHÜSSLING, G. Histological changes in cervical carcinoma in patients receiving cystostatic treatment before hysterectomy. *German. Med. Monthly*, Nov., 1968, *13*, 341–342. (Address: Dr. med. habil. G. Möbius, Bezirkskrankenhaus, Schwerin, Germany.)

Seventy-four patients who underwent radical surgery for Stages I–III cervical carcinoma were studied.

Thirty-seven had been treated by surgery alone, the other 37 received intravenous cyclophosphamide both pre- and postoperatively. The average total dose was between 3,000 and 5,000 mg.

The surgical specimens were examined by two independent pathologists for morphologic effects of this cytostatic treatment. Previously described changes including hydration of the nucleus, "toxic" nuclear changes and blurring of cell borders were found in both treated and untreated specimens alike.

Postoperative complications were present to a higher degree in the treated (38 per cent) than in the untreated (16 per cent) group. The authors feel that this is due to inhibition of wound healing by the cyclophosphamide and advise against this form of preoperative therapy.—*Howard West, M.D.*

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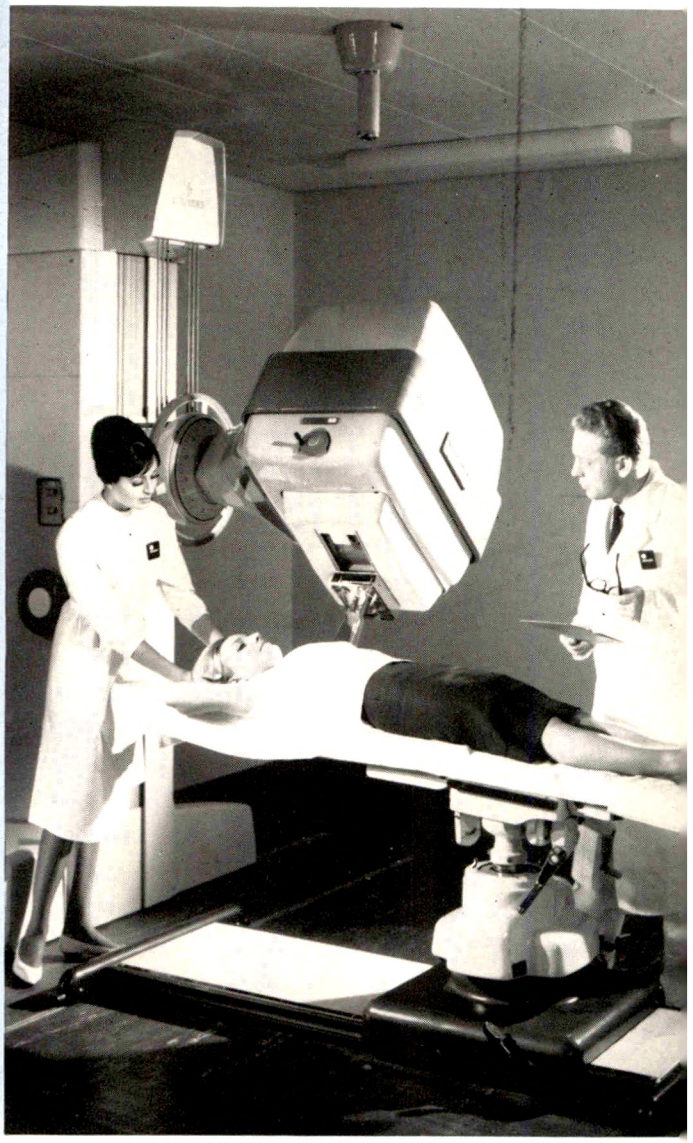
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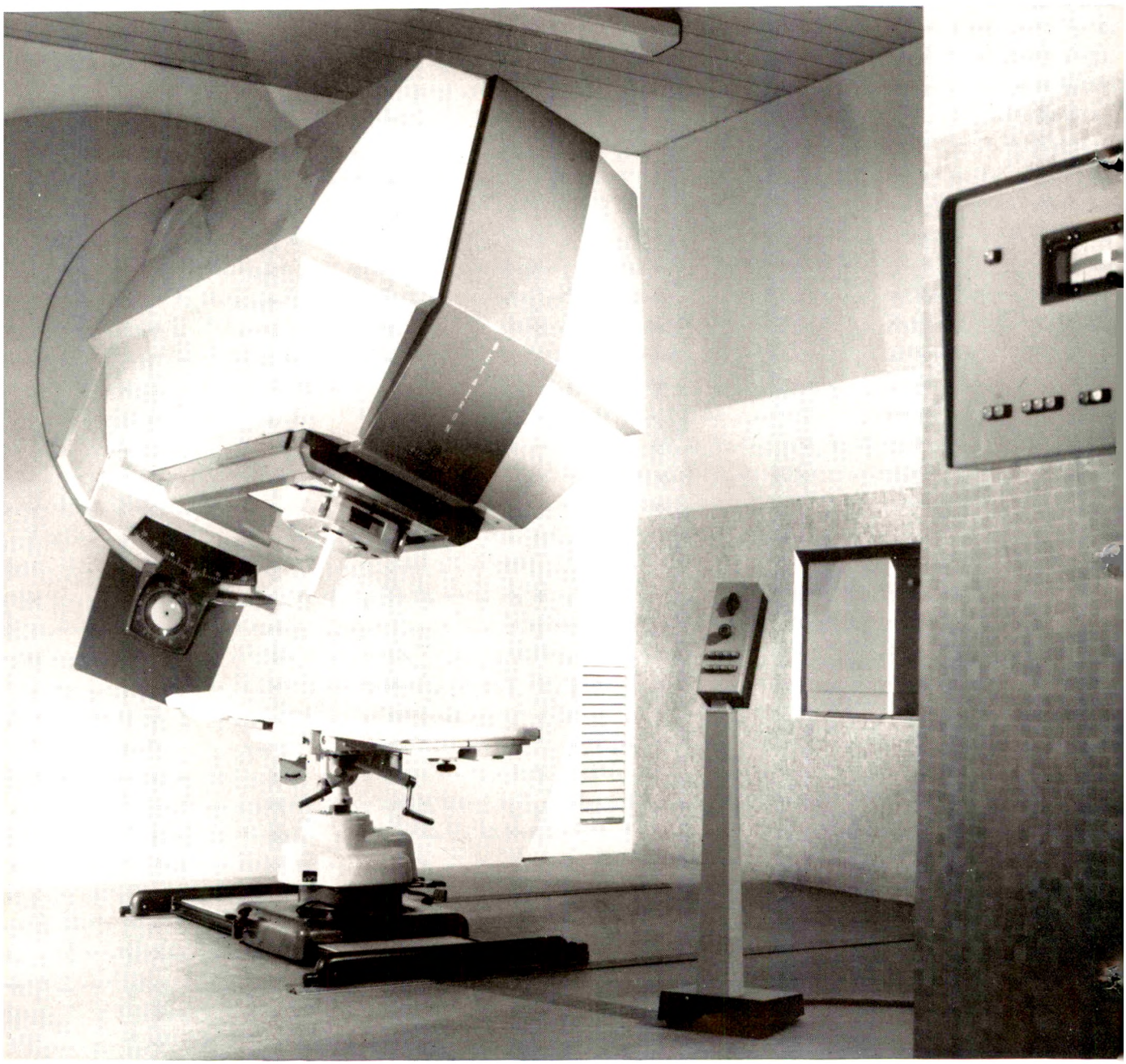


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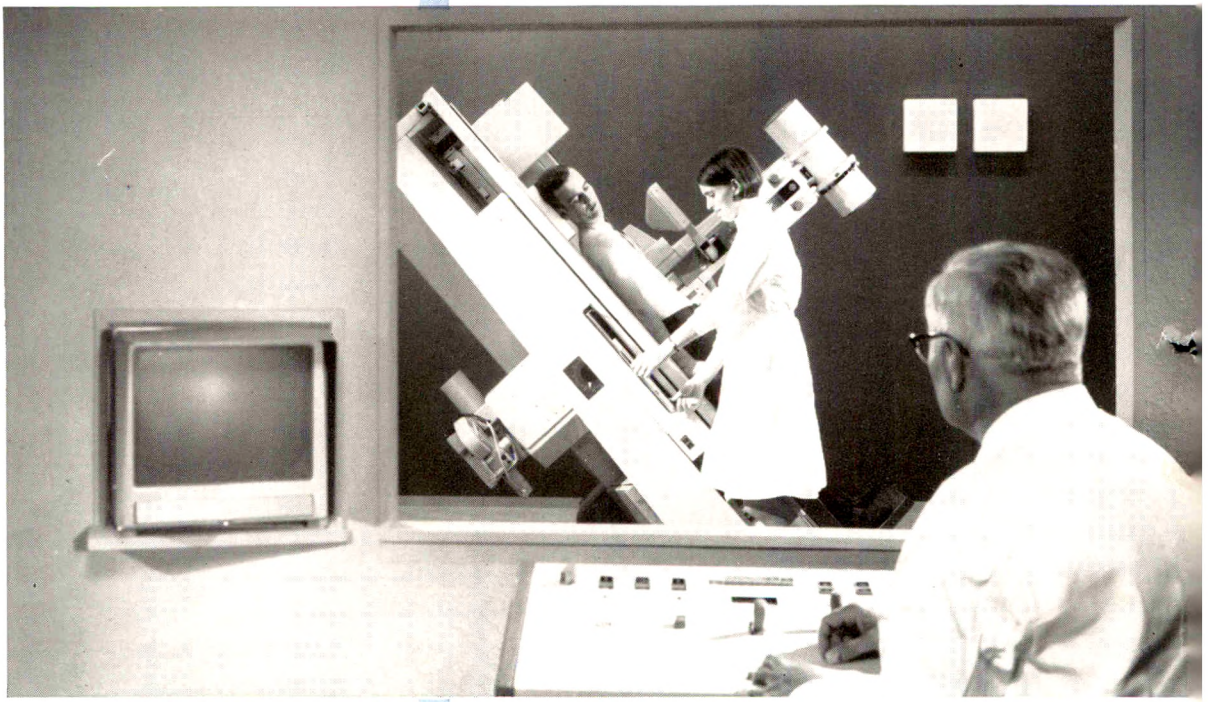
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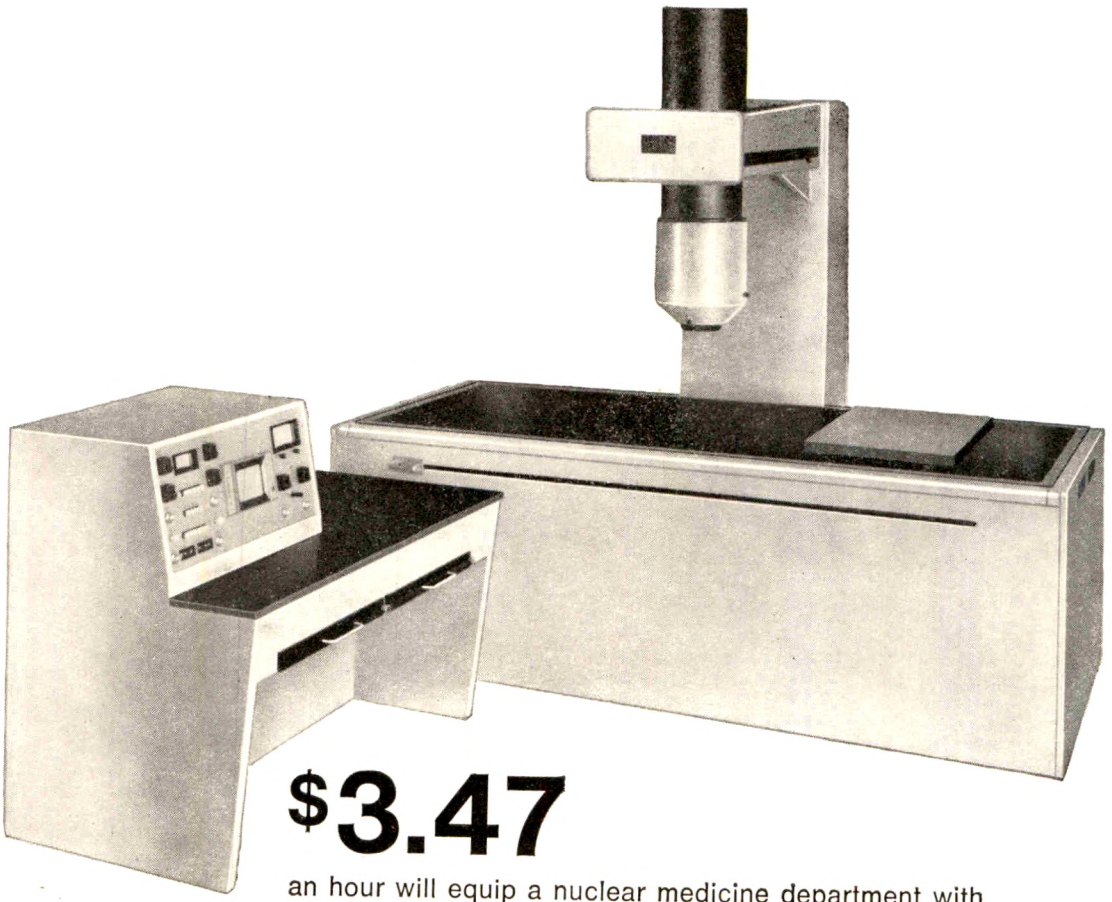
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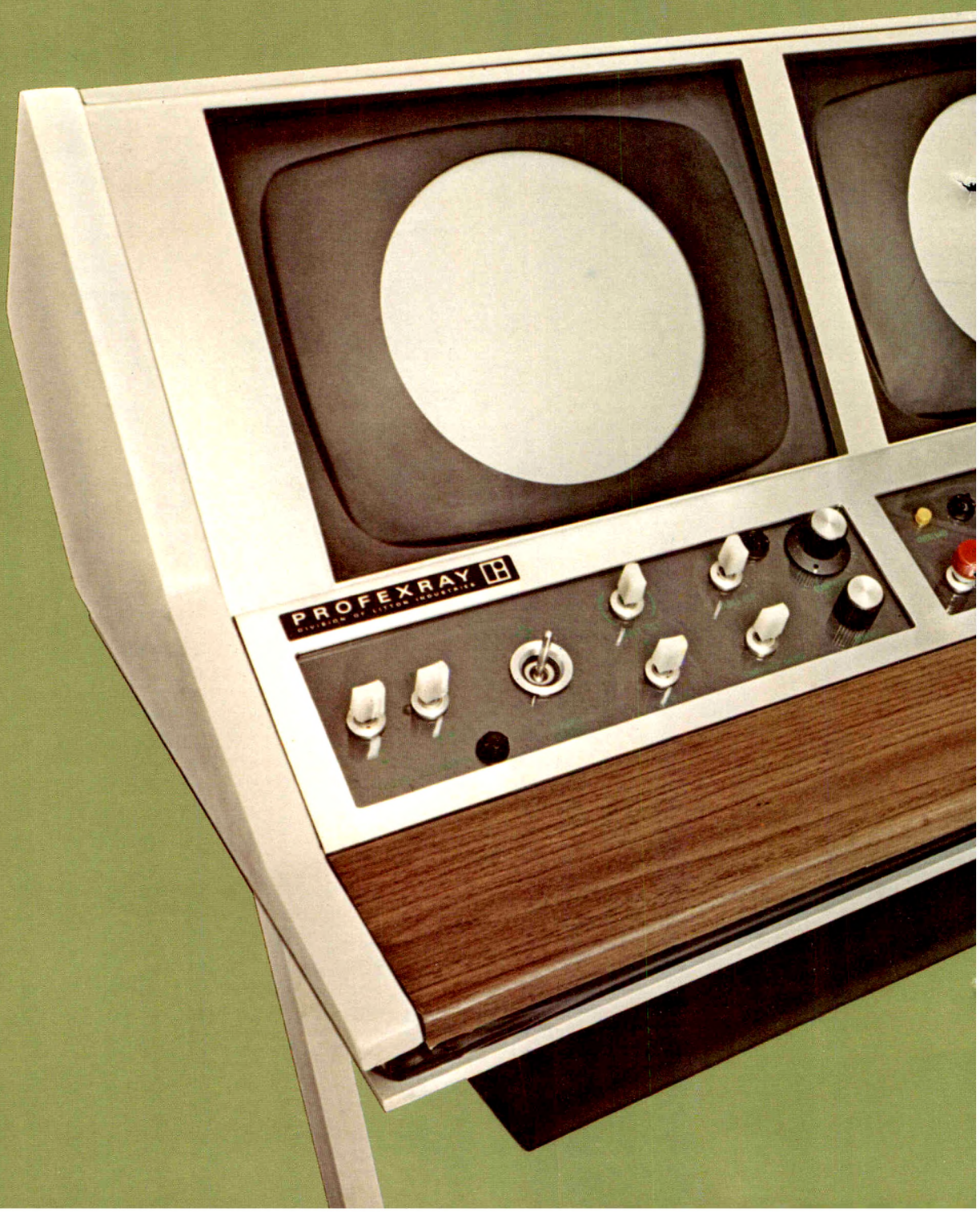
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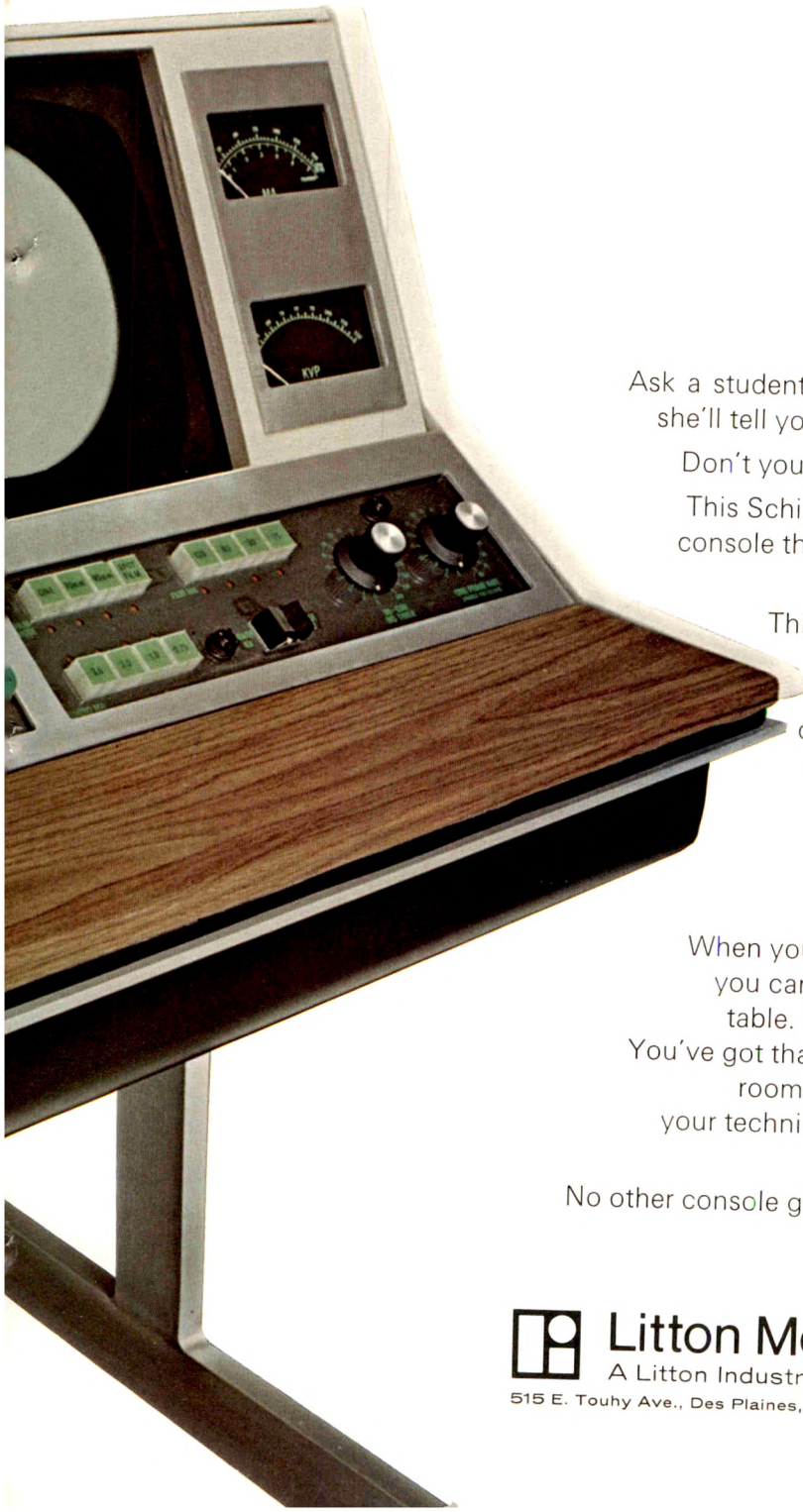
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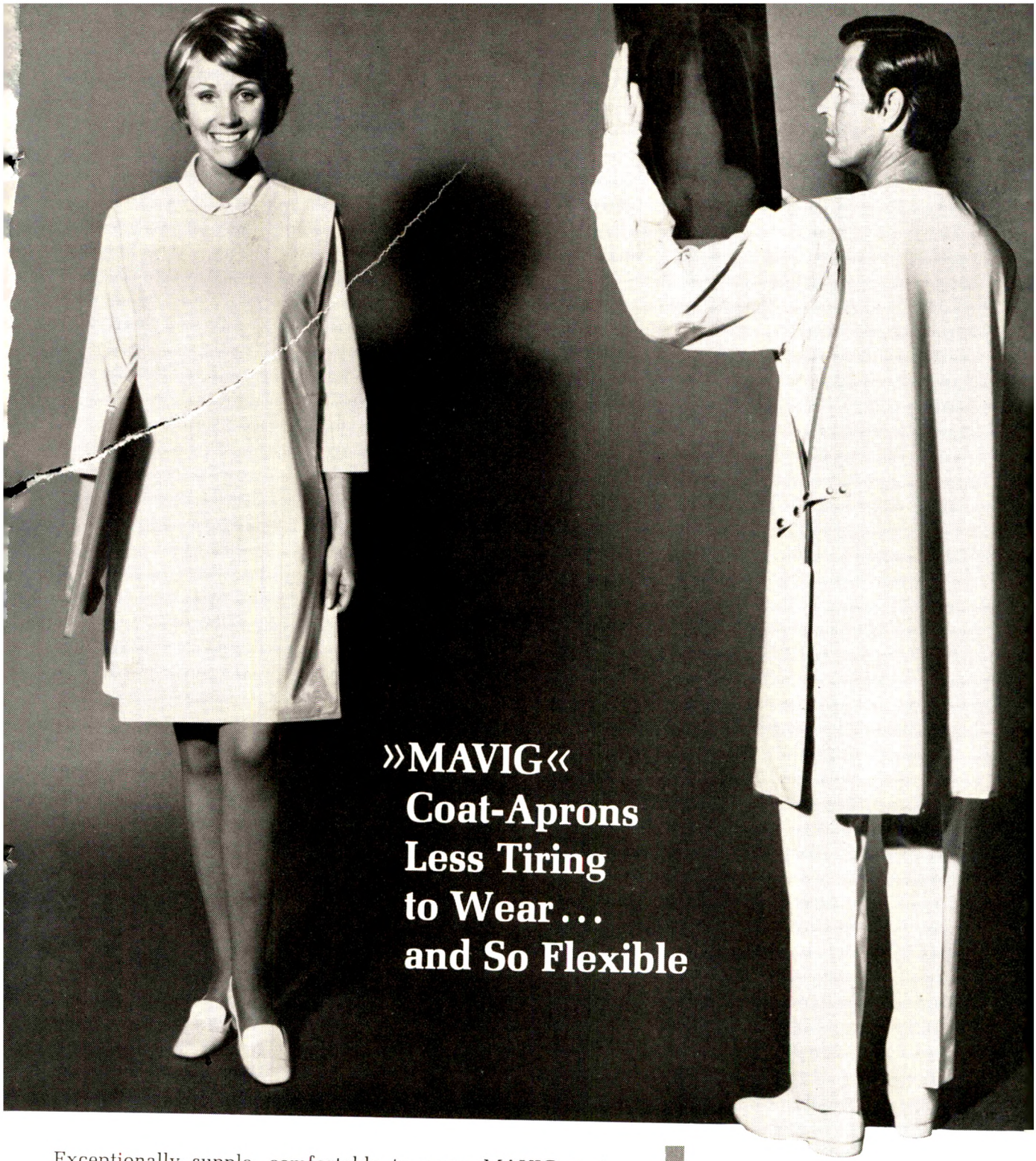
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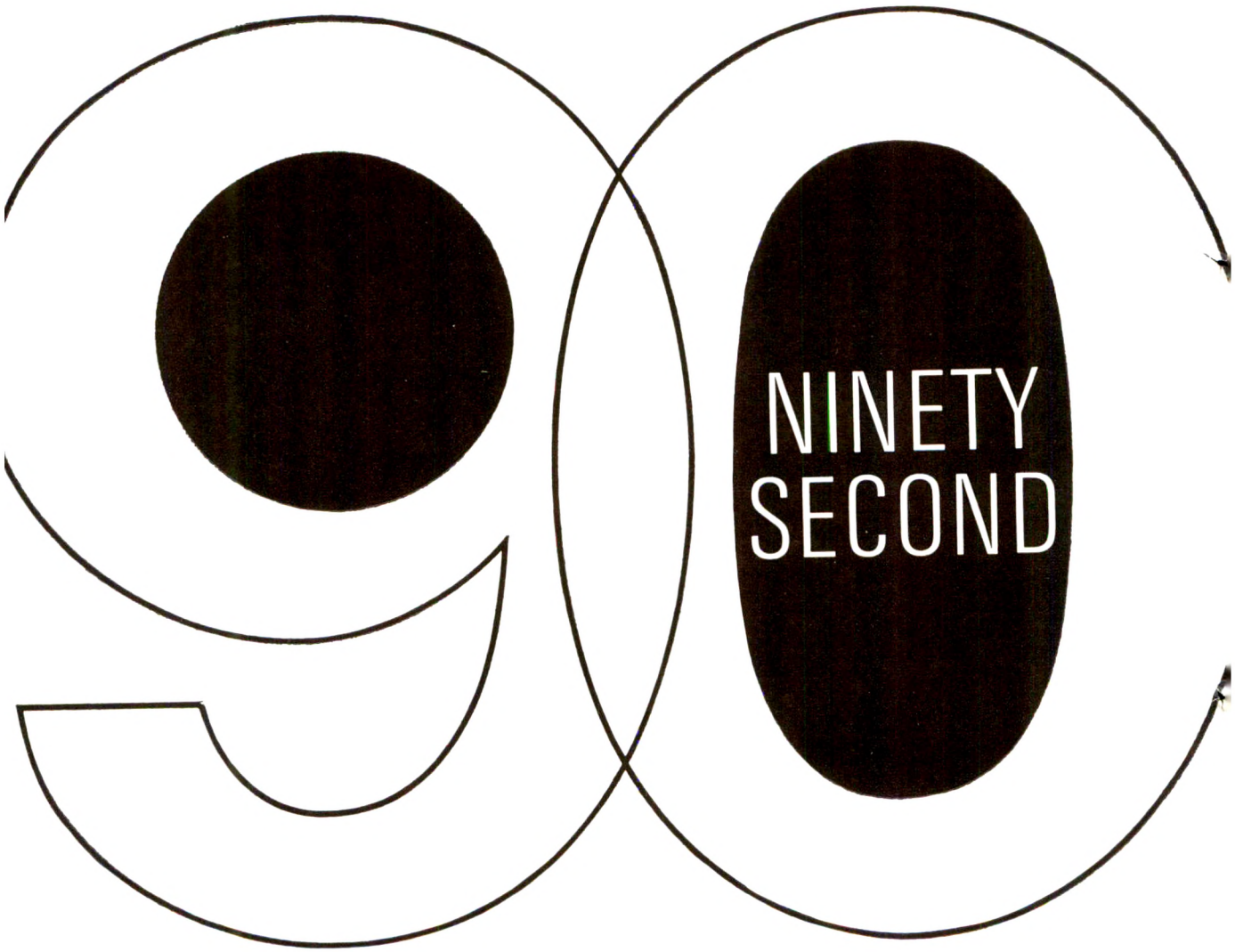
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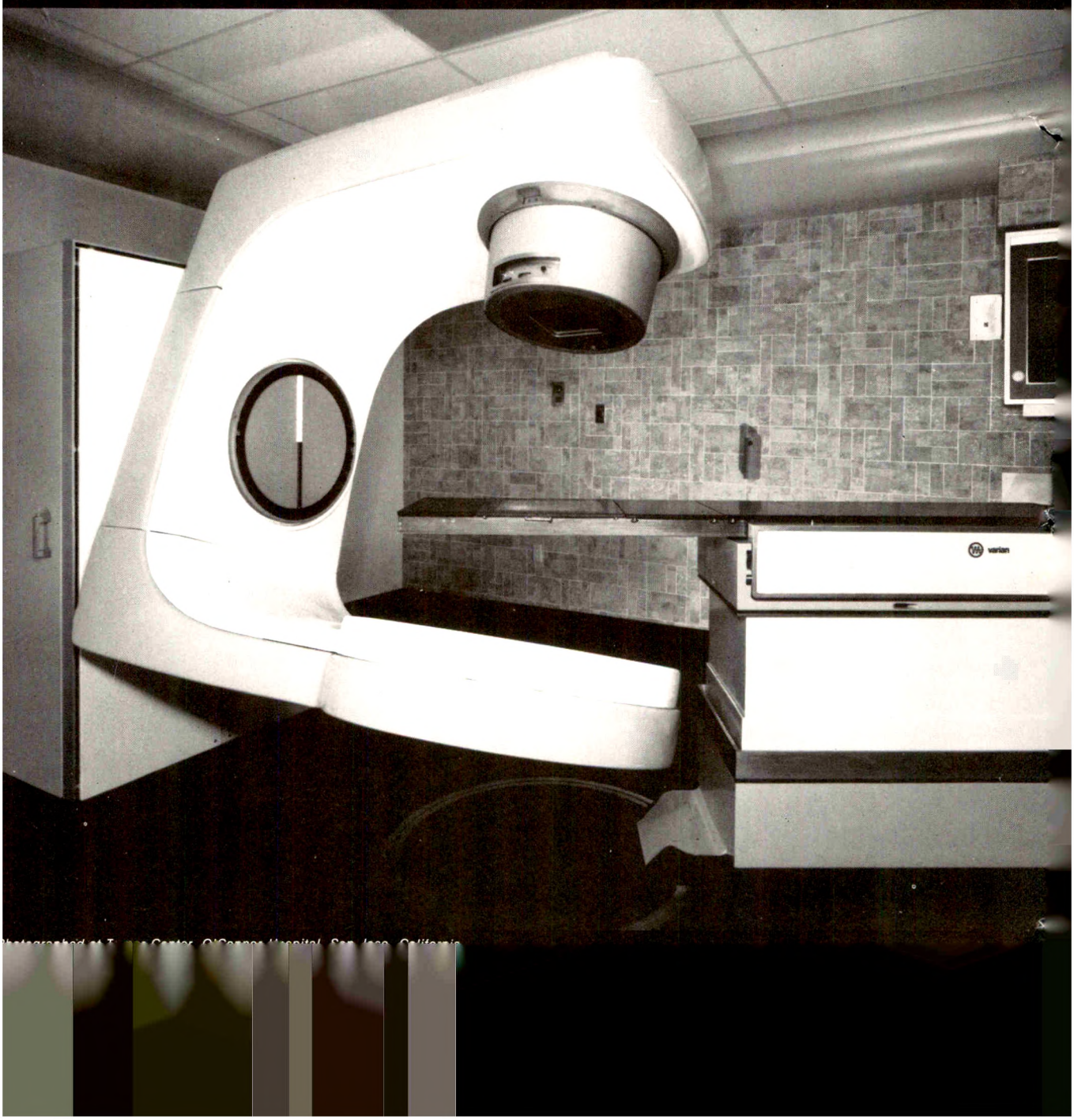
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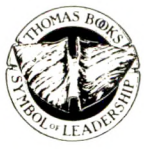
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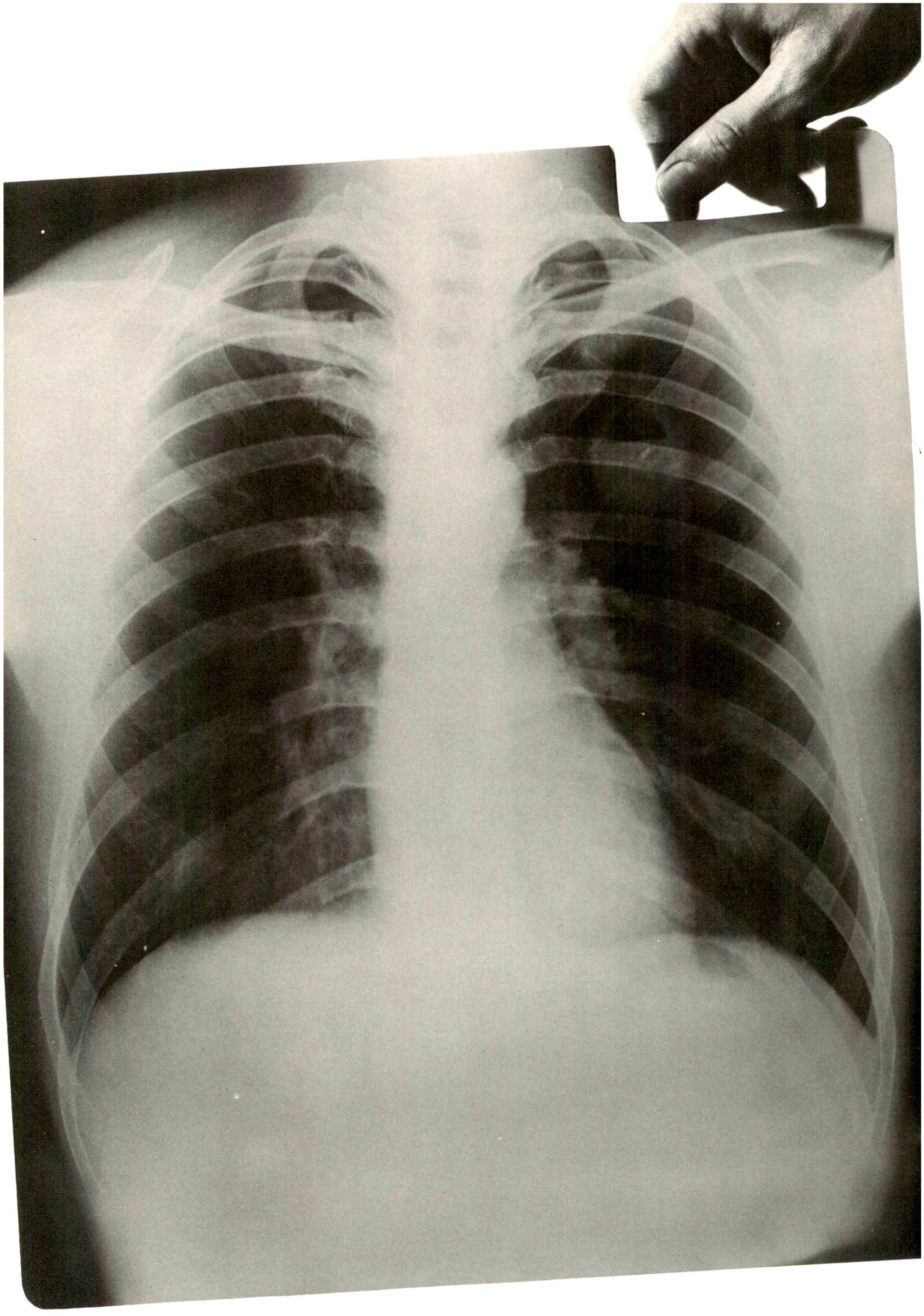
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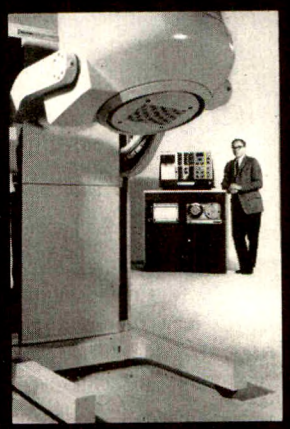


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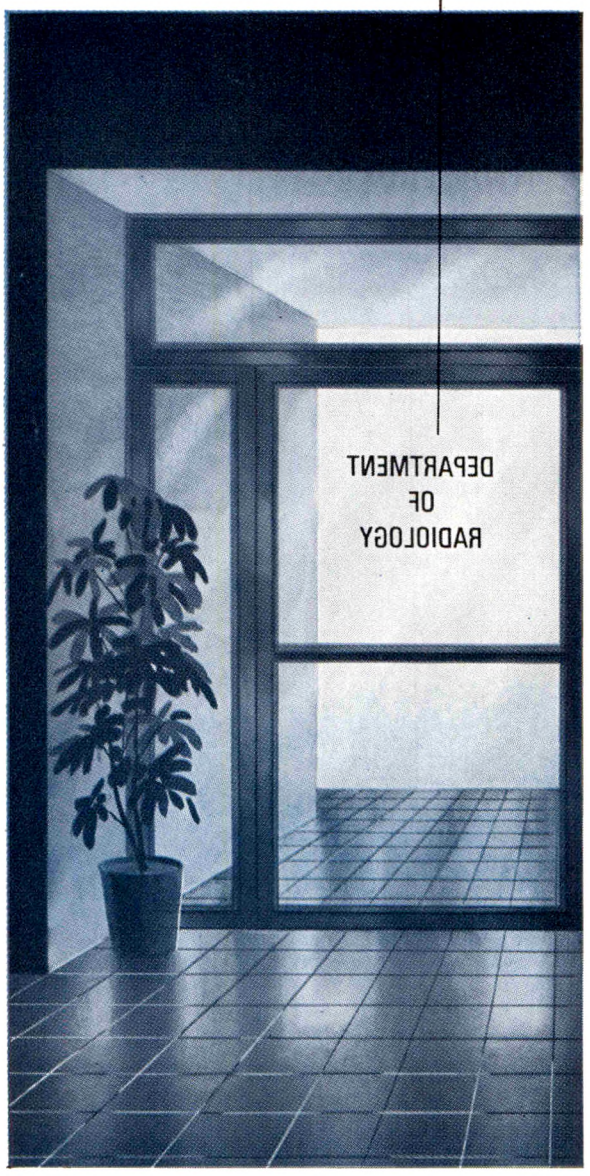
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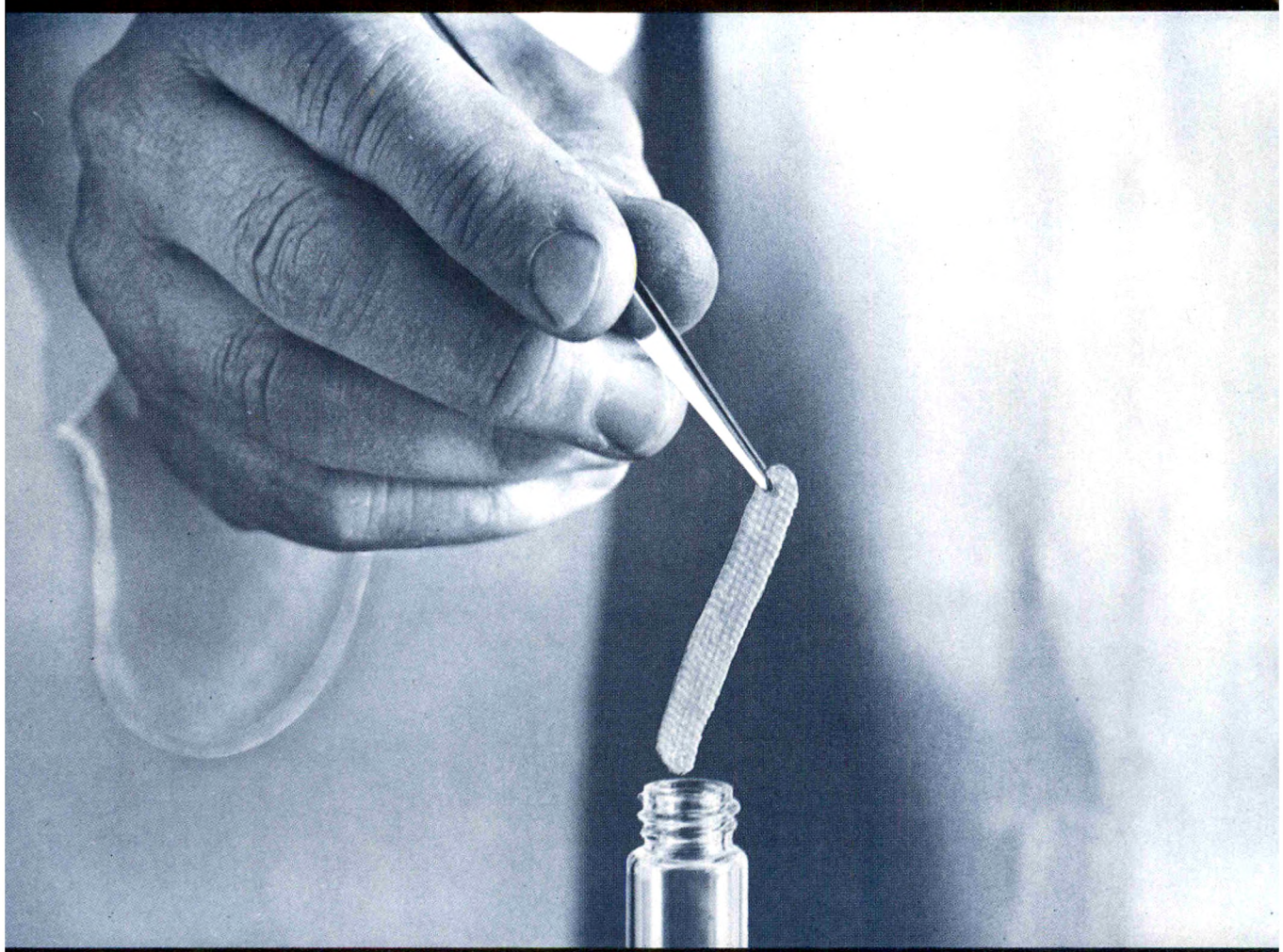
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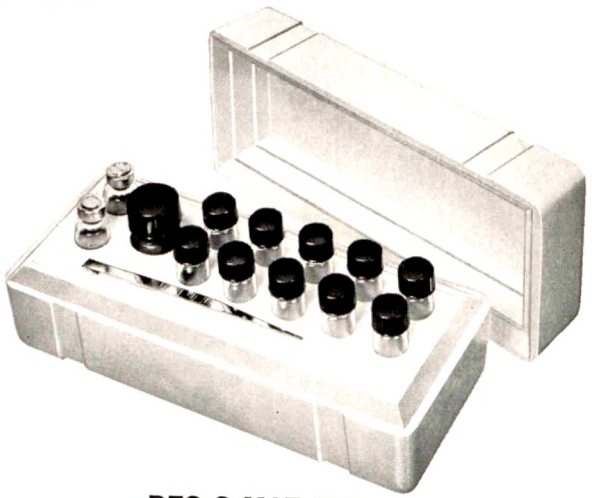
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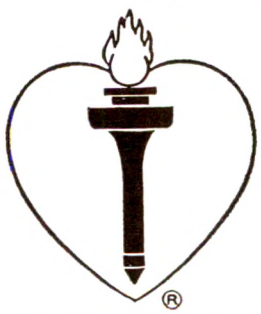
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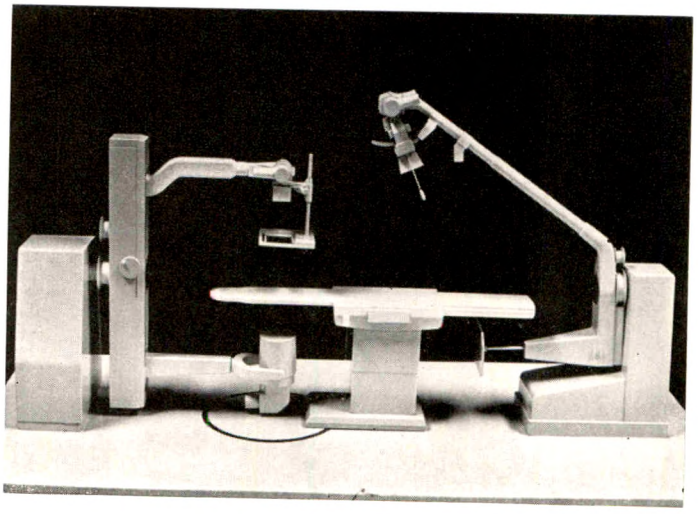
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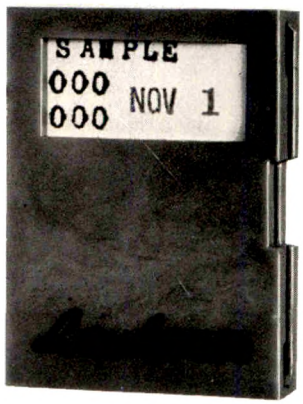
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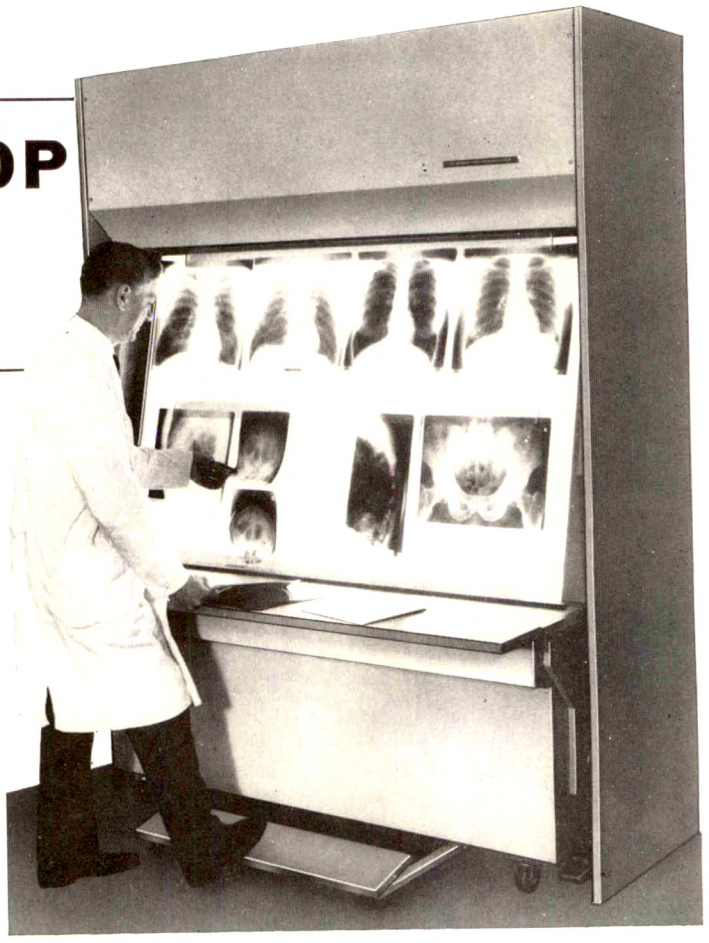
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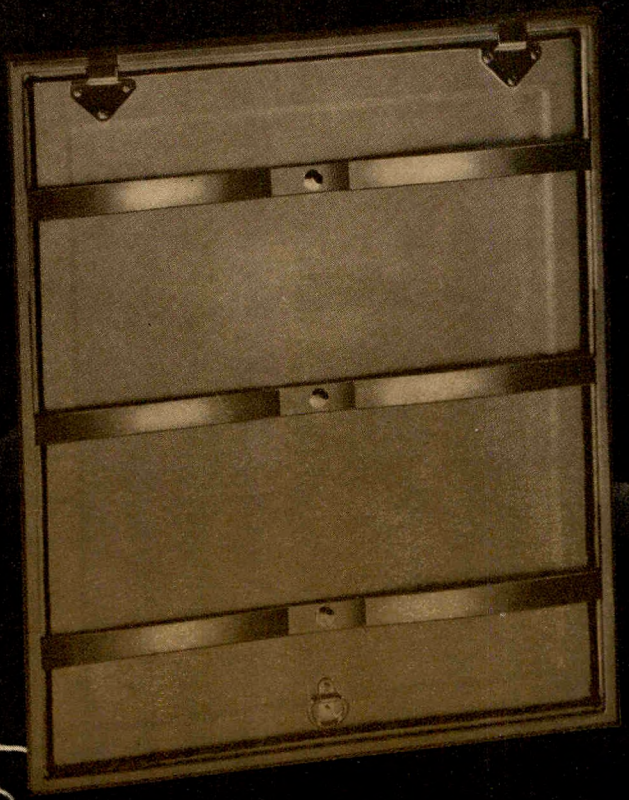
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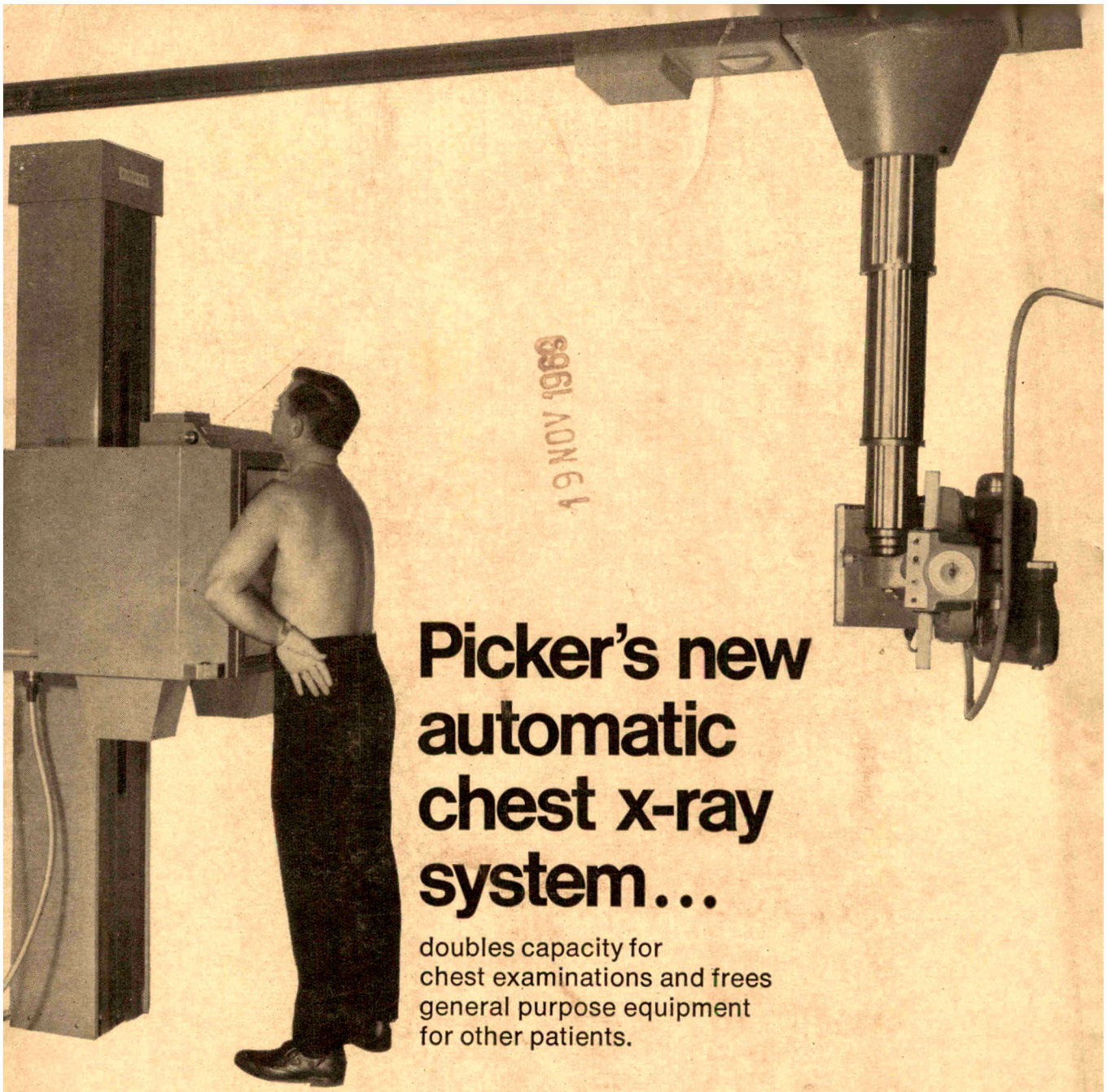
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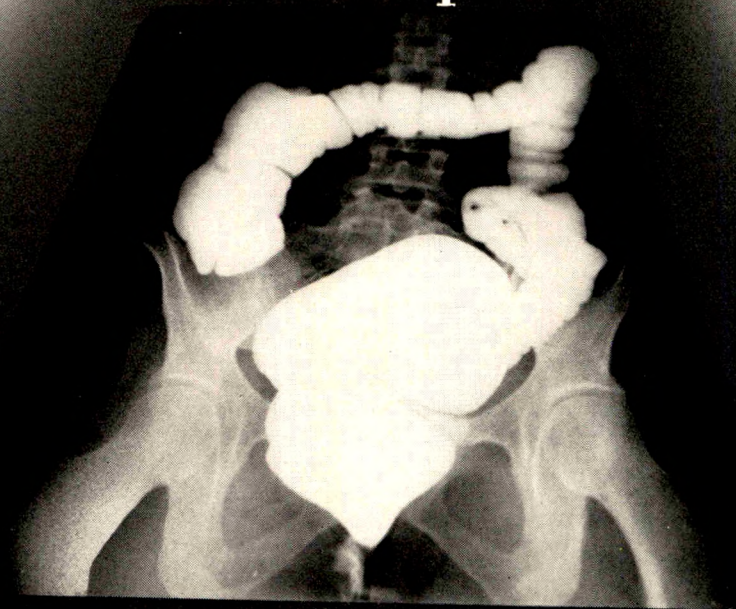
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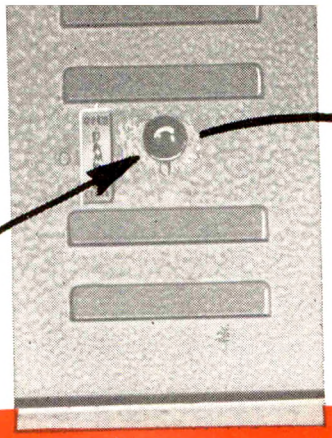
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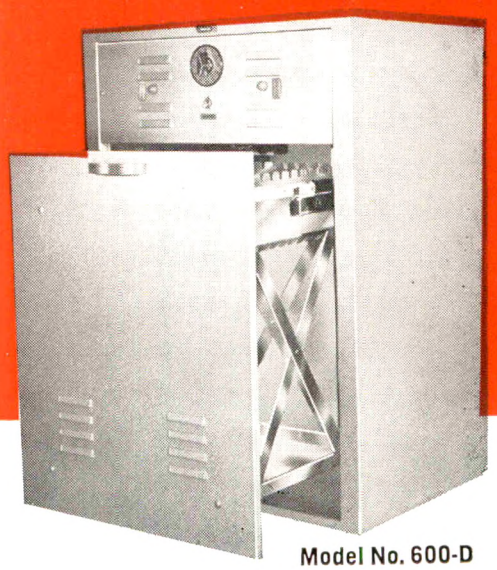
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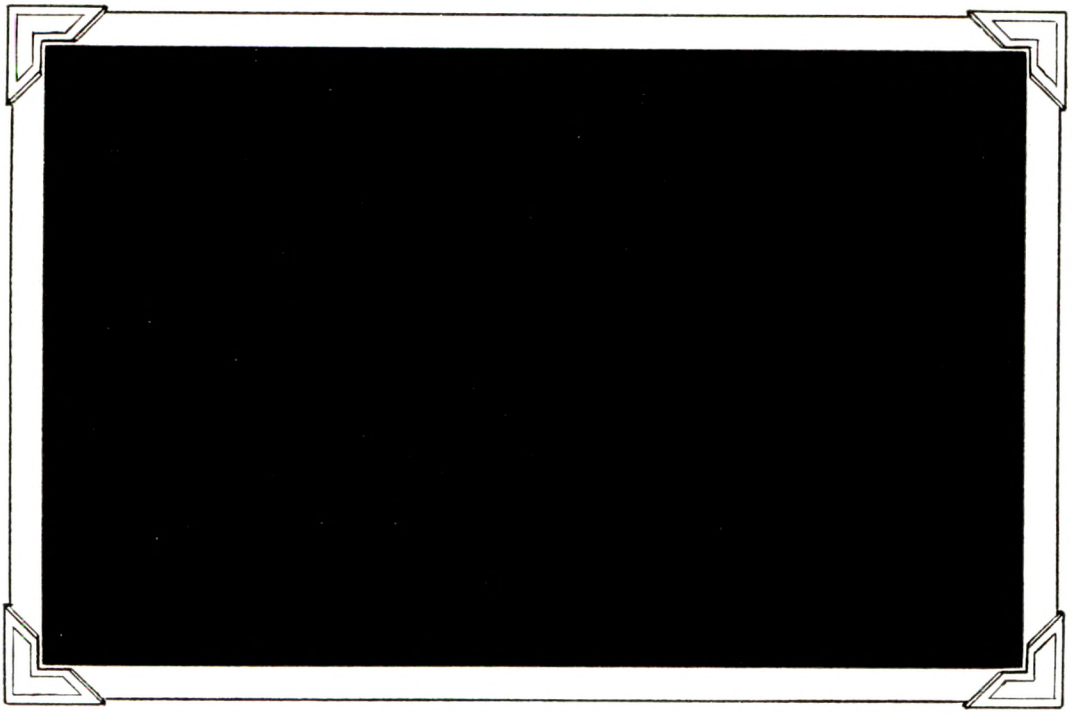
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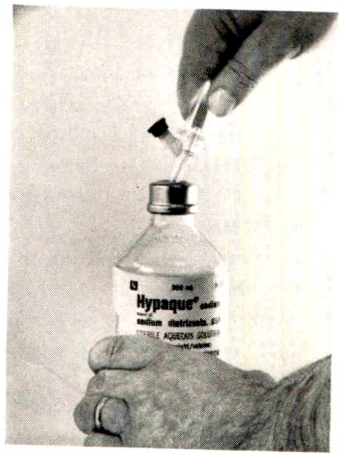
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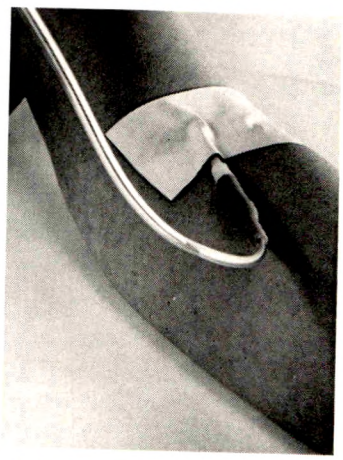
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Insert



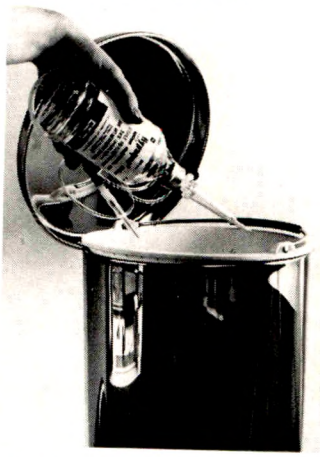
Insert piercing spike of infusion set through rubber stopper of 300 ml. infusion bottle

Infuse



Infuse into an antecubital vein over a period of 3 to 10 minutes

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Discard entire unit when infusion is completed

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- 300 ml. bottle of Hypaque sodium 25% (brand of sodium diatrizoate 25%)
- does not require further dilution
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Diagnostic advantages

- dense prolonged nephrogram facilitates tomography
- physiologic action without distortion
- reduces need for retrograde urography with its inherent dangers
- kidneys, pelves, ureters and bladder usually seen on same film
- permits nephrotomography, urography and cystourethrography with one infusion
- compression and dehydration not always essential

Tolerance

- 300 ml. dose usually as well tolerated as the conventional dose for intravenous urography
- no significant changes of BUN reported after use in patients with impaired renal function

*using regular sterile technique

please see following page for summary of prescribing information

Hypaque® 25% (brand of sodium diatrizoate 25%)
sodium
Sterile Aqueous Injection

PRECAUTIONS

Before a contrast medium is injected, the patient should be questioned for a history of allergy. Although a history of allergy may imply a greater than usual risk, it does not arbitrarily contraindicate the use of the medium. Premedication with antihistamines to avoid or minimize possible allergic reactions may be considered. **Benadryl®** (brand of diphenhydramine hydrochloride), **however, may cause precipitation when mixed in the same syringe with Hypaque sodium.** The injection of 0.5 ml. to 1 ml. of the contrast medium intravenously approximately 15 minutes prior to injection of the full dose is frequently used in an effort to detect patient sensitivity. The absence of a reaction to this test dose is not entirely reliable for predicting the patient's response to the full diagnostic dose. Severe reactions, including fatalities, have occurred with a test dose as well as with larger doses. Adequate facilities for treating severe reactions should be available.

Caution is advised in patients with severe cardiovascular disease and in patients with a history of bronchial asthma or other allergic manifestations or of sensitivity to iodine.

Contrast media have been shown to promote the phenomenon of sickling in individuals who are homozygous for sickle cell disease when the material is injected intravenously or intraarterially.

Water-soluble iodinated radiopaque media will cause a marked elevation of the protein-bound iodine (PBI) level and possibly a false low iodine uptake result up to 48 hours after their use. Therefore, thyroid function studies (PBI and 24-hour radioiodine uptake levels) should be performed prior to radiographic studies, if clinically indicated.

Hypaque sodium 25 per cent should always be administered at body temperature.

Immediate adverse reactions to drip infusion pyelography have not been reported to occur at a higher frequency or greater severity than with routine excretory urography. However, sequelae of this procedure are possible some hours after the examination. Drip infusion pyelography imposes not only a sudden osmotic load, but also may present as much as 160 meq. of sodium (3.7 Gm.) to patients with established, decreased glomerular filtration and renal tubular damage. In addition, these patients may also have coexisting or associated cardiovascular disease. Therefore, the possibility of the development of congestive heart failure hours after the procedure should be considered.

Because of the possibility of inducing temporary suppression of urine, it is wise to allow an interval of at least 48 hours to pass before repeating drip infusion pyelography in patients with unilateral or bilateral reduction of normal renal function.

A definite risk exists in the performance of excretory urography in patients who are known to have multiple myeloma. Partial dehydration in preparation of these patients for the examination is not recommended, since this may predispose to the precipitation of myeloma protein in the kidney tubules.

ADVERSE REACTIONS

Reactions accompanying the use of contrast media may vary directly with the concentration of the substance, the amount used, the technique used, and the underlying pathology.

Adverse reactions, usually of a minor nature, have occurred in 10-14 per cent of patients who have received Hypaque intravenously. Reactions due to **faulty technique** include hematomas and ecchymoses following extravasation from the vein, and pyrogenic reactions. **Hemodynamic reactions** include vasodilatation with flushing, hypotension and, rarely, vein cramp or thrombophlebitis. Serious **cardiovascular reactions** include rare cases of cardiac arrhythmias (e.g., ventricular fibrillation), shock, and cardiac arrest. Transient proteinuria may occur occasionally following the injection of radiopaques and, rarely, oliguria and anuria (renal shutdown) have been reported as a secondary effect of a hypotensive reaction. **Allergic reactions** include asthmatic attacks, nasal and conjunctival symptoms, dermal reactions such as urticaria and, rarely, anaphylactic shock, sometimes with fatal outcome. Severe reactions may also be manifested by signs and symptoms relating to the **respiratory system** (dyspnea, cyanosis, pulmonary or laryngeal edema), or to the **nervous system** (restlessness, confusion, or convulsions). **Other reactions** include nausea, vomiting, excessive salivation, anxiety, headache, and dizziness. Infrequently, "iodism" (salivary gland swelling) from organic compounds appears two days after exposure and subsides by the sixth day.

DOSAGE AND ADMINISTRATION

The recommended dose is calculated on the basis of 2 ml. of Hypaque (sodium diatrizoate) sodium 25 per cent per pound of body weight. The average dose of the solution for adults is 300 ml.; for optimum results, a minimum dose of 250 ml. should be used. A maximum dose of 400 ml. is generally sufficient for the largest of subjects.

The solution is administered intravenously through an 18-gauge needle over a period of three to ten minutes. Pyelographic films are taken at 10, 20, and 30 minutes from the beginning of the infusion. Early 2, 3, 4, and 5 minute films are obtained when indicated for the evaluation of hypertension. Nephrotomographic sections are best taken just at the end of the infusion, and voiding cystourethrograms when desired are usually made at 30 minutes.

HOW SUPPLIED

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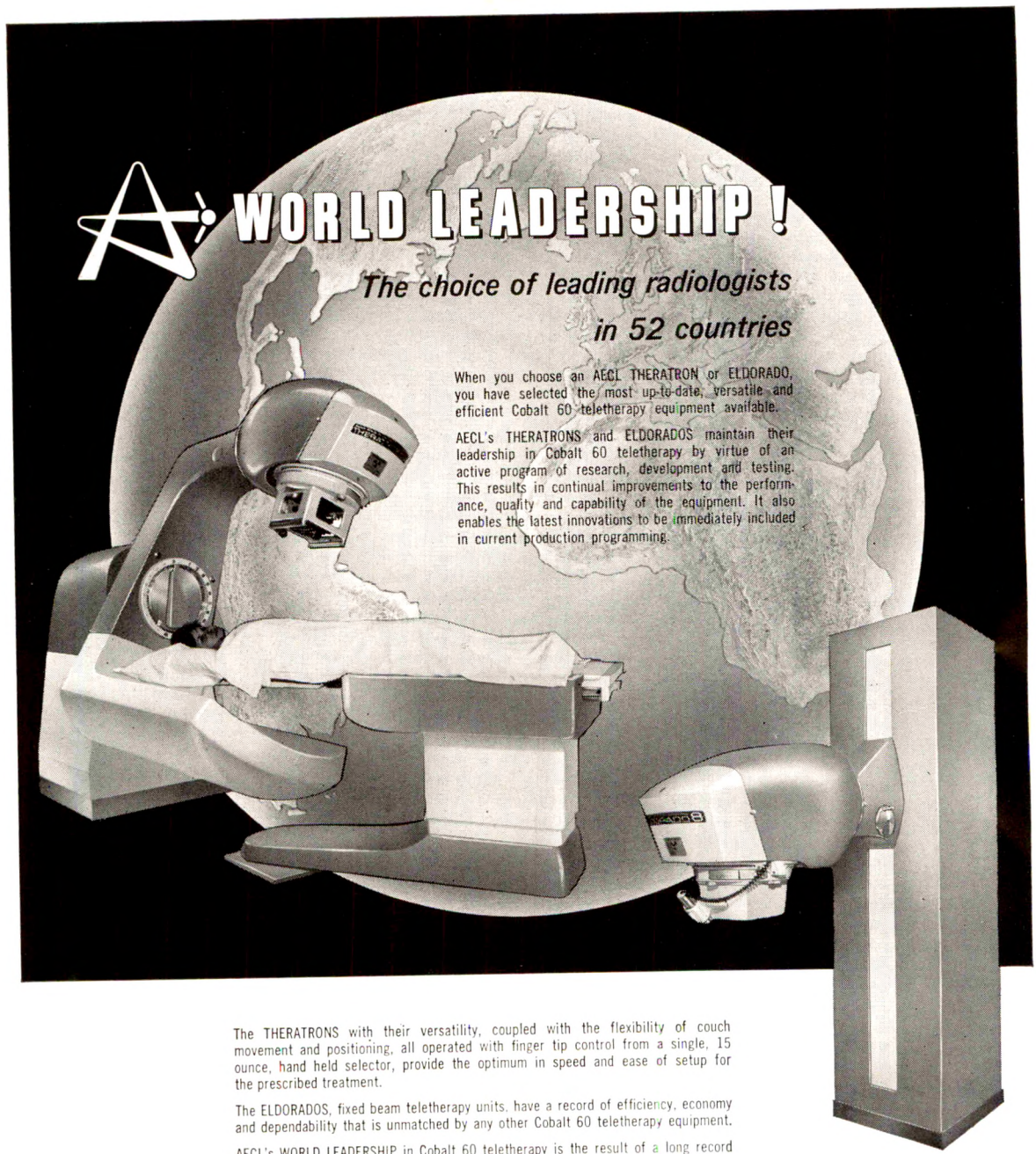
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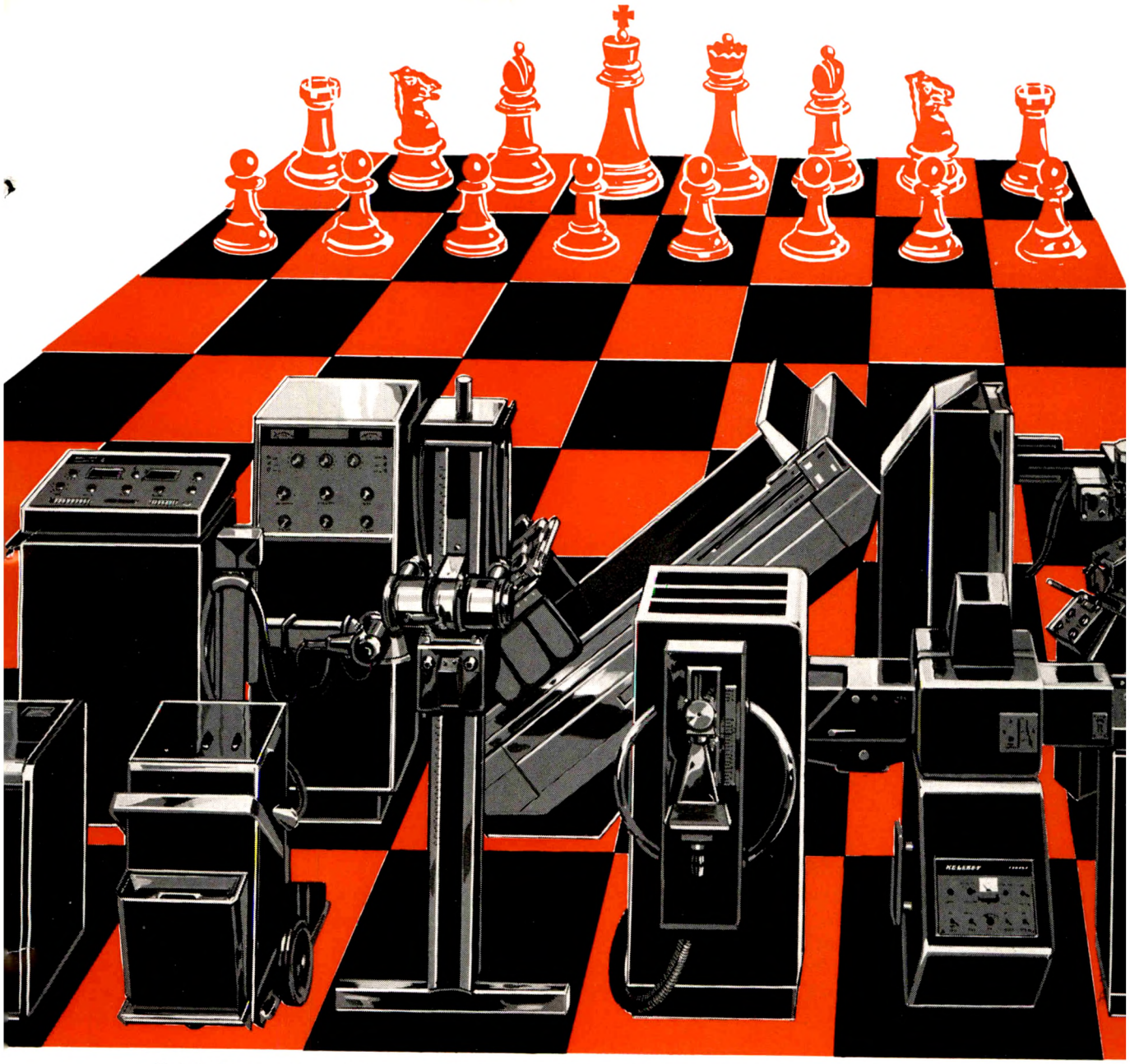
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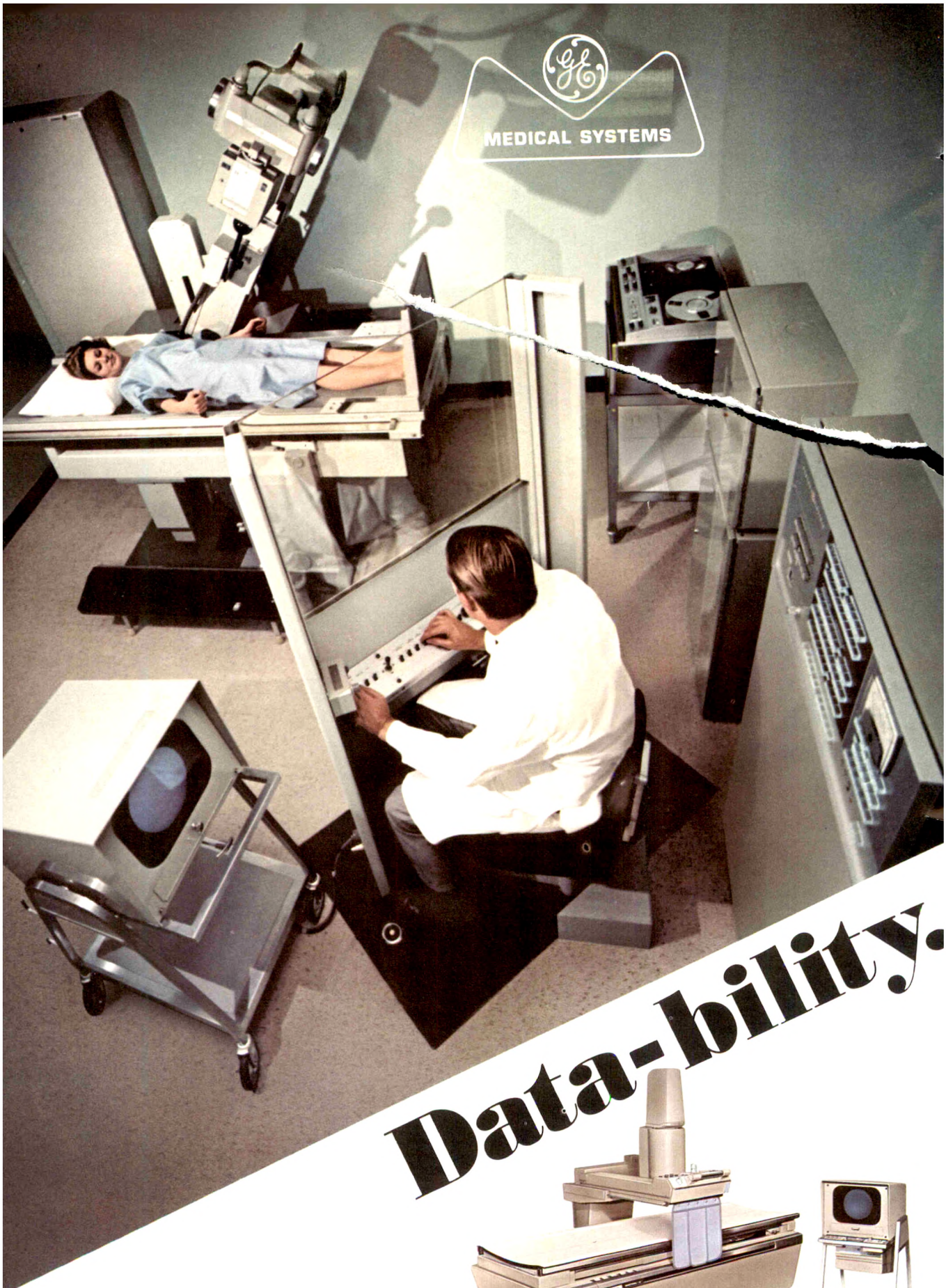
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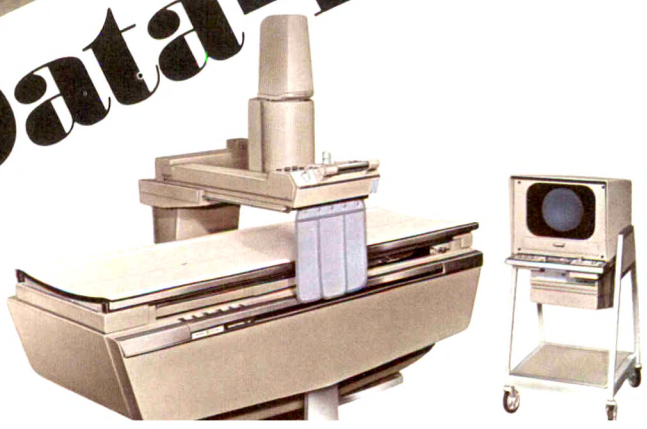
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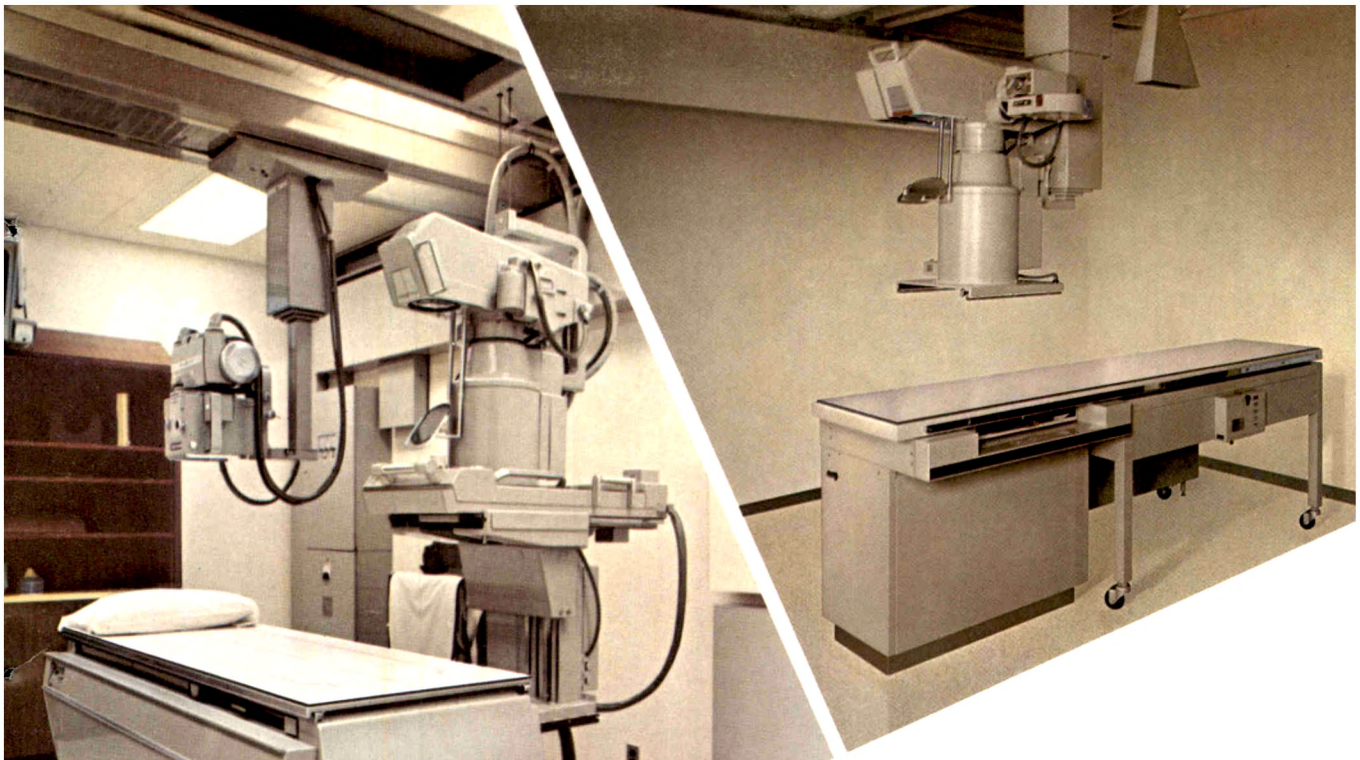


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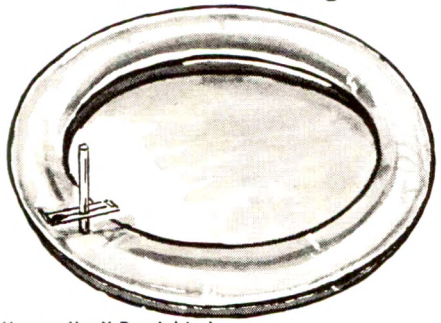
Your GE representative can recommend the equipment combination that gives your hospital Total Information Capability. Talk with him soon.

GENERAL ELECTRIC

MILWAUKEE, WIS. 53201

New Products from E-Z-EM.

Disposable Barium Enema Ring



Use on the X-Ray table to catch spillage.

Keeps table and floor clean.

Use with underpad inside ring and change pad with each patient.

If patient completely evacuates throw entire ring away.

Ring is easily inflated.

No objectionable X-Ray shadow.

Order Catalogue No. 820

Available from your authorized E-Z-EM Dealer.
E-Z-EM, 111 Swalm Street, Westbury, N.Y. (516)333-8230

New Products from E-Z-EM.

X-Ray Wipe Giant size Antiseptic Germicidal Towelette



Order Catalogue No. 500

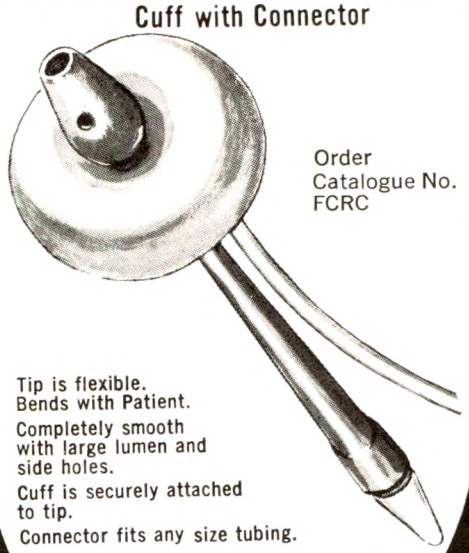
A new economical, convenient way to clean and disinfect patient contact surfaces after every X-Ray examination.

Packaged in handy service boxes 50 per box, 10 boxes per shipping carton.

Available from your authorized E-Z-EM Dealer.
E-Z-EM, 111 Swalm Street, Westbury, N.Y. (516)333-8230

New Products from E-Z-EM.

New Disposable Flexible Retention Cuff with Connector



Order Catalogue No. FCRC

Tip is flexible. Bends with Patient.

Completely smooth with large lumen and side holes.

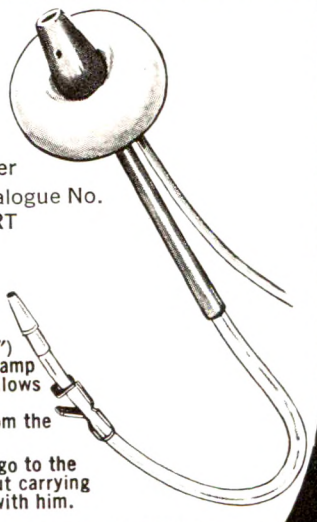
Cuff is securely attached to tip.

Connector fits any size tubing.

Available from your authorized E-Z-EM Dealer.
E-Z-EM, 111 Swalm Street, Westbury, N.Y. (516)333-8230

New Products from E-Z-EM.

New Disposable Flexible Retention Cuff with extended tubing and connector



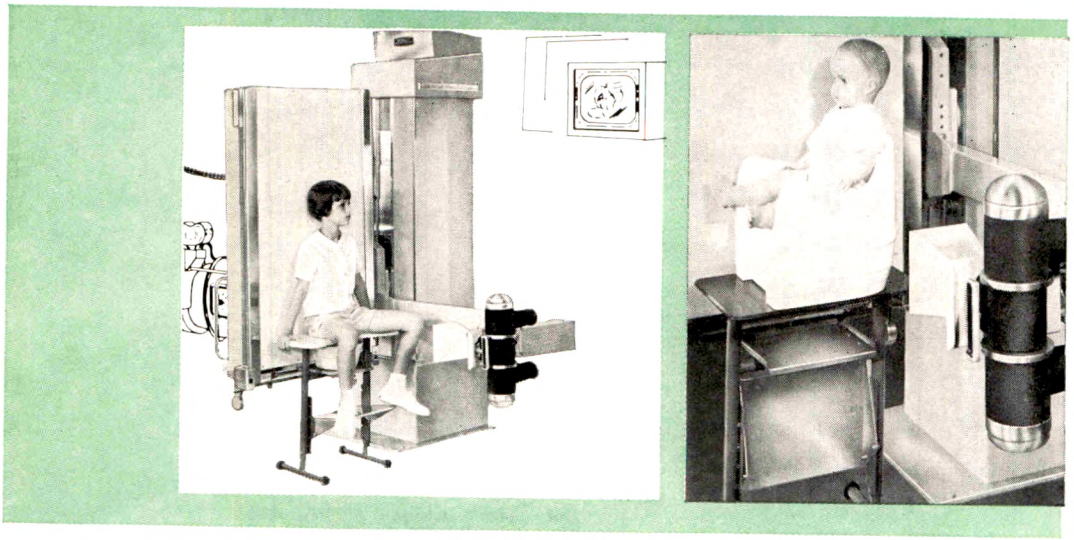
Order Catalogue No. FCRT

Extra length (18") of tubing with clamp and connector allows the cuff to be disconnected from the enema bag.

The patient can go to the bathroom without carrying the enema bag with him.

Available from your authorized E-Z-EM Dealer.
E-Z-EM, 111 Swalm Street, Westbury, N.Y. (516)333-8230

Cuffs alone and cuff on conventional rigid tip also available.

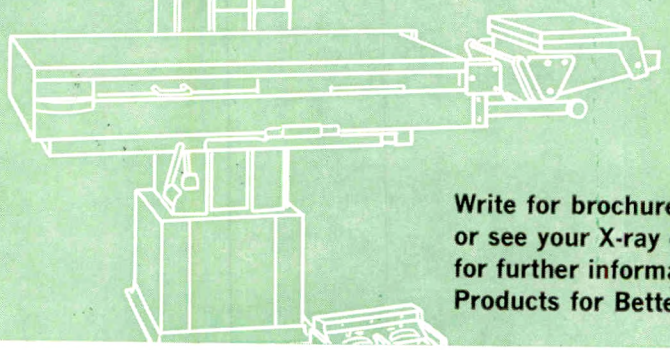


EXTREME UPRIGHT POSITION FOR VOIDING CYSTOURETHROGRAPHY
DURING TELEVISION VIEWING OR RADIOGRAPHY

. . . note voiding stool (optional) for female patients and infants

...another way that the L-F HYDRADJUST TABLE keeps you UP-TO-DATE with the latest in urological techniques!

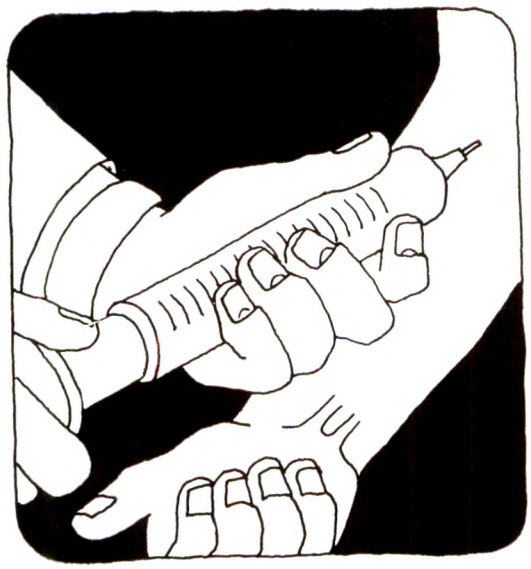
All the modern L-F innovations for Hydradjust Tables, like the voiding cystourethrographic stools shown above, are adaptable to new tables and those tables already in use.



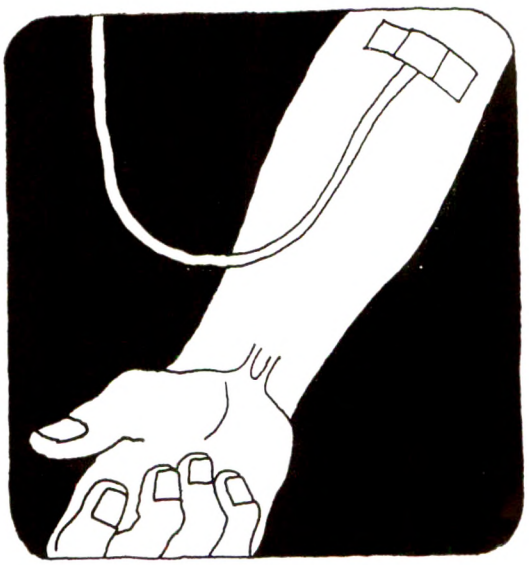
Write for brochures or see your X-ray equipment supplier for further information.
Products for Better Health from Sybron

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SYBRON CORPORATION
CINCINNATI, OHIO 45215 • U.S.A

Now...2 important I.V. Radiodiagnostic procedures for improved visualization



Adequate Dose Urography
with 50-60 ml. of 50% solution



Drip Infusion Pyelography
using between 250-400 ml. of a 25% solution*

Hypaque® 50%

sodium

brand of **sodium diatrizoate**

Winthrop

PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS

*By diluting the 50% solution with an equal amount of sterile water for injection, USP, sodium chloride injection, USP, or dextrose injection, 5%, USP.

(Please see summary on following pages)

Hypaque® 50%
sodium
brand of **sodium diatrizoate**

Excretory Urography and Drip Infusion Pyelography

Description: Hypaque sodium is a sterile aqueous solution of sodium 3,5-diacetamido-2,4,6-triiodobenzoate, a radiopaque medium used to delineate internal structures.

Warning: Do not use Hypaque sodium for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

General and Specific Precautions: Caution is advised in patients with a history of bronchial asthma, other allergic manifestations, or of sensitivity to iodine; these conditions represent a special risk, though not an absolute contraindication. To avoid or minimize possible allergic reactions, premedication with antihistamines may be considered. Benadryl (diphenhydramine hydrochloride) in the same syringe with Hypaque may result in precipitation. A test dose of contrast medium is not entirely reliable. Severe reactions, including fatalities, have occurred with a test dose as well as with the full diagnostic dose.

Caution is advised in patients with severe cardiovascular disease. In patients with impaired renal function and cardiovascular disease, drip infusion pyelography imposes a sudden osmotic and sodium load which can precipitate congestive heart failure. Contrast media injected into arteries or veins can promote sickling of red cells in susceptible individuals. In patients with reduced renal function, repeat of excretory or retrograde pyelography should be delayed at least 48 hours to avoid temporary suppression of urine. In preparation for excretory urography of patients with multiple myeloma, partial dehydration is not recommended, since this may predispose to the precipitation of myeloma protein in the kidney tubules. When thyroid function studies (PBI and 24-hour radioiodine uptake levels) are indicated, they should be performed *prior* to radiographic studies or several days afterwards, to avoid inaccurate results.

Hypaque sodium 50% should always be injected at body temperature.

General and Specific Adverse Reactions: Adverse reactions, usually of a minor nature, have occurred in 10-14 per cent of patients who have received Hypaque intravenously. Reactions due to *faulty technique* include hematomas and ecchymoses, following extravasation from the vein, and pyrogenic reactions. *Hemodynamic reactions* include vasodilatation with flushing, hypotension and, rarely, vein cramp or thrombophlebitis. Serious *cardiovascular reactions* include rare cases of cardiac arrhythmias (e.g., ventricular fibrillation), shock, and cardiac arrest. Transient proteinuria may occur occasionally following the injection of radiopaques and, rarely, oliguria and anuria have been reported secondary to a hypotensive reaction. *Allergic reactions* include asthmatic attacks, nasal and conjunctival symptoms, cutaneous reactions such as urticaria and, rarely, anaphylactic shock, sometimes with fatal outcome. Severe reactions may also be manifested by signs and symptoms relating to the *respiratory system* (dyspnea, cyanosis, pulmonary or laryngeal edema), or to the *nervous system* (restlessness, confusion, or convulsions). *Other reactions* include nausea, vomiting, excessive salivation, anxiety, headache, and dizziness. Infrequently, "iodism" (salivary gland swelling) from organic compounds appears two days after exposure and subsides by the sixth day. Reactions to drip infusion pyelography may not appear until some hours after the examination.

Angiography (Peripheral Arteriography and Venography)

Precautions *(See also General Precautions):* Extreme caution is advised in considering peripheral arteriography in patients suspected of having thromboangiitis obliterans (Buerger's disease). Any procedure (even needling or insertion of a catheter) may induce a severe arterial and/or venous spasm. Caution is also advisable in patients with severe ischemia associated with ascending infection.

Adverse Reactions *(See also General Adverse Reactions):* In addition to those listed under General Adverse Reactions, are those due to arterial trauma during the procedure (i.e., needling, insertion of catheter, subintimal injection, perforation, etc.) as well as to the hypertonicity or effect of the medium; also reported are transient arterial spasm, extravasation, hemorrhage, hematoma with tamponade, injury to nerves proximal to artery, thrombosis (rare in venography; if vein is irrigated following injection), dissecting aneurysm, arteriovenous fistula, (e.g., with accidental perforation of femoral artery and vein during needling) transient leg pain from contraction of calf muscles in femoral arteriography; transient hypotension after intraarterial (brachial) injection, and brachial plexus injury with axillary artery injections.

Cerebral Angiography: Because of the special techniques required, it is recommended that Hypaque sodium be used for this purpose only by persons skilled and experienced in carrying out this procedure.

Contraindication: Carotid angiography should be avoided during the progressive period of a stroke, since this increases the risk of cerebral complications.

Precautions *(See also General Precautions):* Select patients for this procedure with care. Use the 50 per cent solution with caution in extreme senility (but not old age, *per se*); advanced arteriosclerosis; severe hypertension; and cardiac decompensation.

The diagnostic value of the procedure, according to many authorities, when employed early enough in locating lesions amenable to surgery, may outweigh the added risk to patients who have recently experienced cerebral embolism or thrombosis (stroke syndrome). A small number of postangiographic fatalities, including progressive thrombosis, have occurred in which the procedure did not appear to play a role. Patients with severe cerebrovascular disease may be examined primarily by indirect methods of angiography.

Care should be exercised to avoid contaminating catheters, syringes, needles, and contrast media with glove powder or cotton fibers.

Angiography is hazardous in subarachnoid hemorrhage. In migraine, the procedure can be hazardous because of ischemic complications, particularly if performed during or soon after an attack.

Adverse Reactions *(See also General Adverse Reactions):* The major sources of complications are faulty technique, occlusive atherosclerotic vascular disease, repeated injections of the contrast media, and higher doses than those recommended.

Untoward reactions are mostly mild and transient, although permanent visual field defects and deaths have been reported.

(continued on next page)

(continued from preceding page)

Hypaque® 50%
sodium
brand of **sodium diatrizoate**

Vascular reactions: flushing, vessel spasm, thrombophlebitis, and cutaneous petechiae.

Neurologic complications: transient cerebral blindness, neuromuscular disorders, convulsions, coma, hemiparesis, unilateral dysesthesias, visual field defects, aphasia, and respiratory difficulties.

Aortography

Precautions *(See also General Precautions):* Special caution is advised to avoid inadvertent intrathecal injection when using the translumbar technique. The incidence and severity of reactions or complications that may occur are influenced by: the care and experience with which the procedure is performed; the amount and type of medium used; the age and condition of the patient; and the premedication and anesthesia used. Since aortography is not without some danger, it should be performed only by those experienced in the technique. Wherever possible, repeated injections of the solution during a single study should be avoided.

Adverse Reactions *(See also General Adverse Reactions):* Renal damage and shutdown; neurologic complications such as transverse myelitis or paraplegia; cardiovascular complications such as shock, cardiac arrest or failure, coronary occlusion, arterial thrombosis, embolism, and perforation of vessels; extravasation or hemorrhage from the puncture site or retroperitoneal catheter perforation; necrosis of the intestinal wall; acute pancreatitis; deaths; diffuse cutaneous petechiae; subintimal injection and aortic dissection.

Intraosseous Venography

See General Precautions and Adverse Reactions. A general anesthetic is sometimes necessary since the method is painful. Occasionally, extravasation of the contrast medium from the needle into the soft tissue may occur.

Direct Cholangiography

Precaution *(See also General Precautions):* This procedure should be used with caution in the presence of acute pancreatitis, injecting no more than 5 to 10 ml. without undue pressure.

Adverse Reactions *(See also General Adverse Reactions):* These may be attributed to injection pressure or excessive volume of the medium, resulting in overdistention. Such pressure may produce a sensation of epigastric fullness, followed by moderate pain in the back or right upper abdominal quadrant, which will subside when injection is stopped.

Some of the medium may enter the pancreatic duct and cause a transient serum amylase elevation 6 to 18 hours later, without apparent ill effects. Pancholangitis resulting in liver abscess has been reported. Occasionally, nausea, vomiting, fever, and tachycardia have been observed.

Hysterosalpingography

Contraindications: Menstruation, active or imminent; infection in any part of the genital tract, including the external genitalia; pregnancy, known or suspected. Use not advised for six months after end of pregnancy, or 30 days after conization or curettement.

Precaution *(See also General Precautions):* Caution should be exercised in patients with known or suspected carcinoma to avoid possible spread of the lesion by the procedure.

Splenoportography

Precautions *(See also General Precautions):* Procedure should be performed with caution on patients with blood dyscrasias, a tendency to severe bleeding, or a spleen recently become tender and palpable.

Adverse Reactions *(See also General Adverse Reactions):* Persistent hemorrhage with hemoperitoneum has been reported, and, in some instances, hemorrhage has required splenectomy.

How Supplied: Ampuls of 30 ml., boxes of 1, 10, and 25. A 1 ml. sensitivity test ampul is furnished with each ampul. Vials of 20 and 30 ml., rubber stoppered, boxes of 1, 10, and 25. Vials of 50 ml., rubber stoppered, boxes of 1 and 10. Each vial contains sufficient excess to permit withdrawal of 1 ml. for testing sensitivity.

If the solution is chilled, crystals may form but will readily dissolve if the ampul or vial is placed in moderately hot water before use. Cool to body temperature before injecting.

Winthrop

WINTHROP LABORATORIES, New York, New York 10016
PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS



Pakorol-XU "A gem of an x-ray processor"

"Pako has come up with a gem in the Pakorol-XU film processor," says Shirley Merriam, lab technician for three internal medicine and cardiology specialists in Winter Haven, Florida.

"We process about fifty 14 x 17″ radiographs a week on the Pakorol-XU and the quality is always good. There's no comparison to any other manual or automated method I've used. And the 90-second dry-to-dry time speeds up diagnoses and eliminates the element of error in reading wet film," Shirley added.

The Pakorol-XU eliminates messy dripping and spilling of chemical solutions to make x-ray processing one of the cleanest jobs in the medical field, according to Shirley.

"I was concerned about automatic processing at first," she said, "but after 7 months of constant use, we find that the Pakorol-XU is easy to operate and easy to maintain. We just wash the rollers nightly, clean the tanks once a month and change the solution every couple of months."

For more information about the Pakorol-XU, contact your Pako X-Ray Distributor.

PAKO®

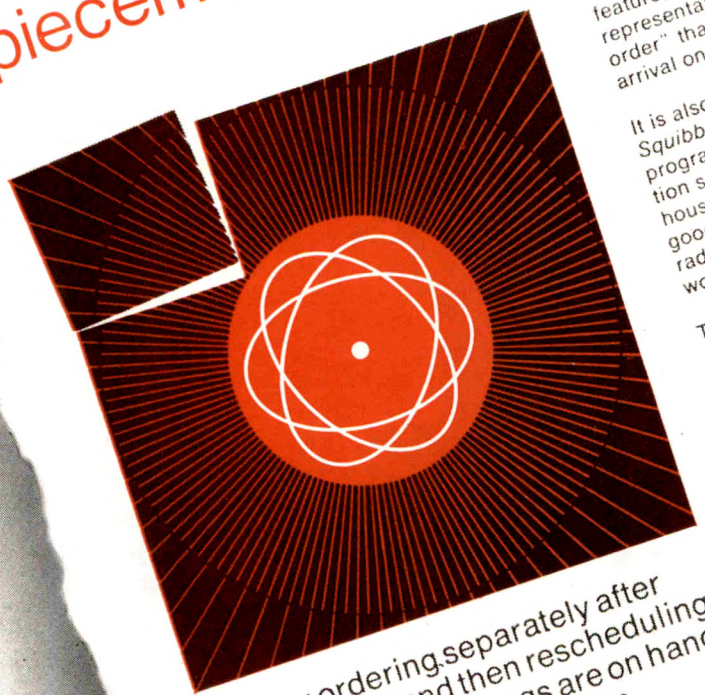
PAKO CORPORATION
6300 Olson Memorial Highway, Minneapolis, Minnesota 55440

PS Processing Systems for the Photographic, Motion Picture, Graphic Arts, Medical and Industrial X-Ray Industries

SQUIBB

a research concept in radiopharmaceuticals

Are you ordering radioisotopes piecemeal?



Are you ordering separately after each referral and then rescheduling the patient? Most drugs are on hand when the patient needs them. Why not radiopharmaceuticals?

If a hospitalized patient needs blood, he can have it within minutes. If an ill patient needs penicillin, it can be prescribed immediately. But if he should need a radio-diagnostic test, he may have to wait several days for the material to arrive.

There was a time when such waiting was necessary, but no longer. Many of the available radiopharmaceuticals have now reached the stage when they can be integrated into the mainstream of medical and hospital practice and can be "at hand" when needed. In particular, the unique 5-day precalibration of Squibb radioisotopes makes the need for ordering separately after each referral a thing of the past. Most laboratories can pretty well estimate what their approximate weekly need will be, so that everything can be ordered in one shipment to arrive on any given day. Thus, when a patient is referred, the diagnostic agent is already on hand and the test can be run immediately. Moreover, there is only one shipping charge. And if the material arrives for use during the latter part of the working week, Squibb will bear the cost of radioactive decay over weekends.

If you want to know more about this unique service feature, please contact your Squibb professional representative. He can arrange for a weekly "blanket order" that is shipped to you automatically for arrival on any day you specify.

It is also important that you know of the unique Squibb "*prefill*" *program* that anticipates and programs radiopharmaceutical parenteral production so that sterility and pyrogen test data are "in house" before the material is released. Thus, Squibb good manufacturing practices assure—even with radiopharmaceuticals—the same high standards you would expect in any regular parenteral preparation.

These are only a few of the many important features and services available to you when you use Squibb radioisotopes. Your Squibb representative will be happy to give you more details.

Medotopes®

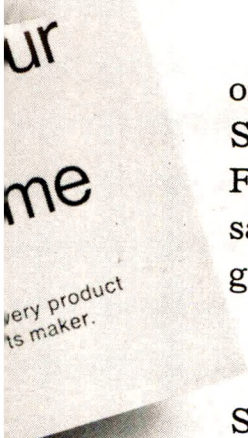
Squibb Radiopharmaceuti

unique 5-day
precalibration
lets you have
entire week
needs at or

SQUIBB 'The Priceless Ing
is the honor and

This Squibb concept was bound to be emulated...

it's much easier to "follow the leader"



Unique service programs are hard to originate. But once established they *can* be emulated. And the unique Squibb 5-day Precalibration Plan was bound to be copied. For it has been eminently successful—offering significant savings in time, trouble and money to laboratories, as well as greater convenience and faster scanning service for patients.

Although others have now followed in our footsteps, reasonable facsimiles are not the original. For the broad Squibb experience and technical know-how that conceived and made the original plan possible has not been surpassed.

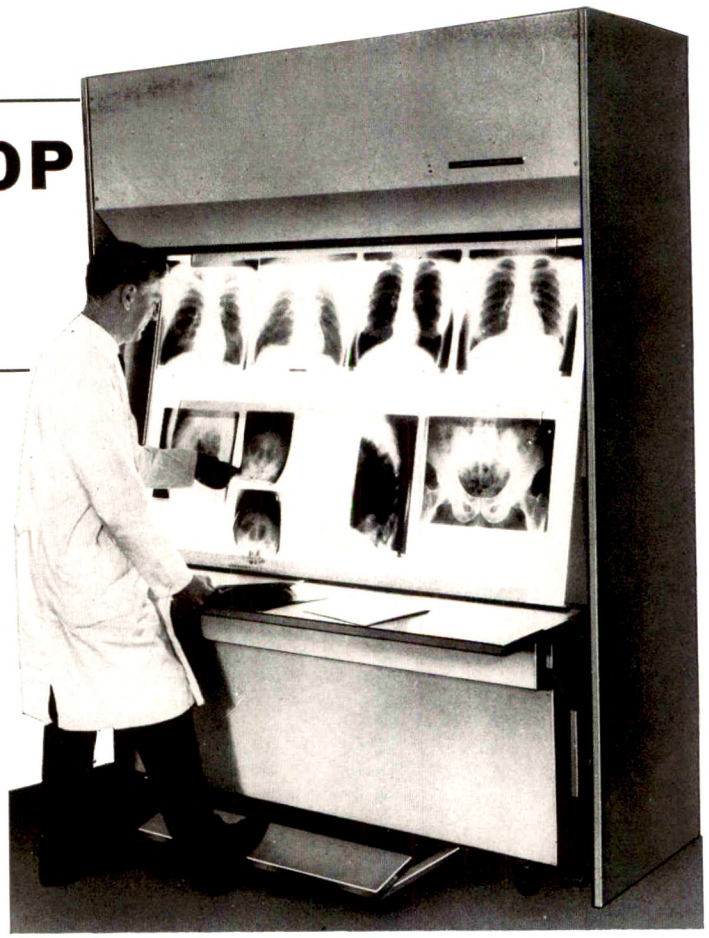
For details on the many important—and frequently unique—features and services available to you when you use Squibb radiopharmaceuticals, contact your Squibb Representative.

Medotopes®

Squibb Division of Nuclear Medicine

ROLLOSKOP

HIGH-CAPACITY FILM VIEWING DEVICE



The Rolloskop introduces a time and work saving method for the display of the X-ray films. It is based on a stationary illuminator unit and a mobile carriage for storage and transport of previously hung films. Identical units should be installed in pre-reading and demonstration rooms.

Immediately after processing, the radiographs for reading are hung on a transparent plastic band provided with clips. This band runs vertically over the illuminated area (57″ × 40″) on to spools in the top of the illuminator unit and in the carriage. The carriage with the films can be disengaged from the illuminator and transported to the viewing room where it is engaged to a second illuminator. Thus the films can be demonstrated in different places without being hung more than once. Radiographs can also be kept in spare carriages, e.g. for teaching purpose. Each spool takes up to 160 14″ × 17″ films.



ELEMA-SCHONANDER, INC.

Post Office Box 130 Mount Prospect, Illinois 60056

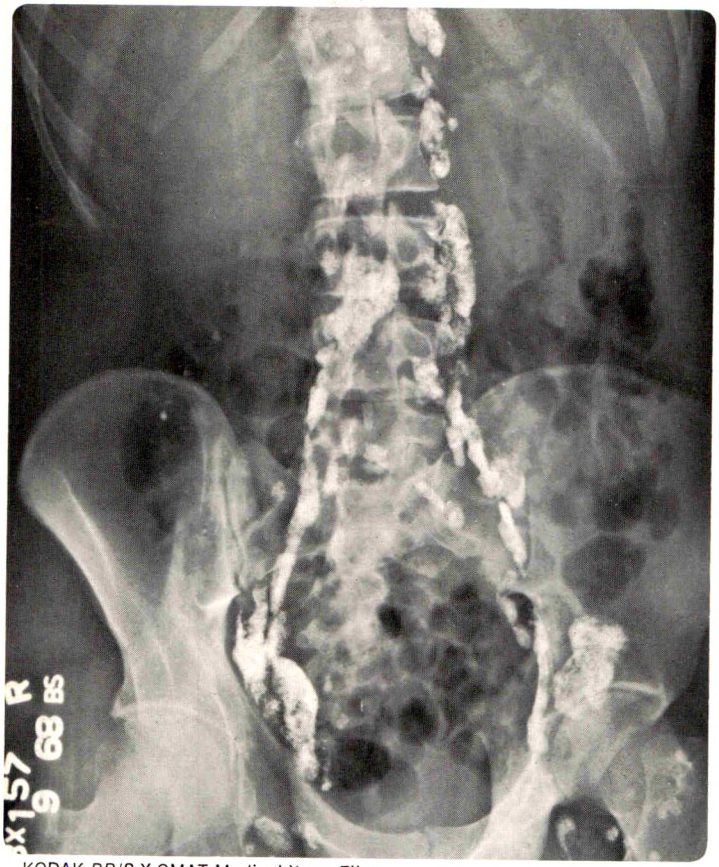
Koda

90 second proof

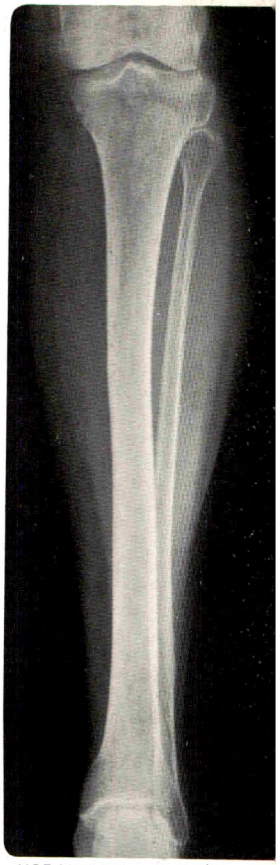


KODAK RP X-OMAT Medical X-ray Film





KODAK *RP/S* X-OMAT Medical X-ray Film—significantly faster for minimum exposure.



KODAK *RP/L* X-OMAT Medical X-ray Film—records the wides range of tissue densities.

KODAK *RP** X-OMAT Films give more information, time after time.

Quality and film choice are the reasons you get radiographs with more information when you use KODAK *RP* X-OMAT Films, Chemicals, Processor.

Film choice is an important part of Kodak quality. Now, there are four KODAK *RP* X-OMAT Films to choose from. Three in standard sheet and roll form; the fourth, a "spot" film with exceptional contrast. No matter which of these films you choose to fulfill your requirements, the result will be more of the information you're after, every time.

Quality processing is another part of the Kodak story. And it's a short one: 90 seconds from exposed film to reading, with the KODAK *RP* X-OMAT Processor and the new system-balanced, long-life Kodak Chemicals.

For more information in your radiographs, select only the x-ray products that bear the name KODAK *RP* X-OMAT.

Kodak

*Rapid Processing

EASTMAN KODAK COMPANY

Laurel *and* Hardy. Inseparable. Made for each other.

The same goes for a nuclear-medicine department. Only *one* imaging system goes with it—is made for it—brings the department to its full potential.

Some things simply belong together.

Only the Pho/Gamma® III Scintillation Camera by Nuclear-Chicago. Only the Pho/Gamma III has the in-vivo visualization capabilities, the full range of data displays and data-manipulation accessories for today—and tomorrow.

Which is why more and more nuclear-medicine departments are going with and growing with the Pho/Gamma III. And helping to make it, now more than ever, *the world's most experienced scintillation camera.*

Call your Nuclear-Chicago sales engineer. Or write to us for full details on the Pho/Gamma III. 9-215



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CULVER PICTURES

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HIS DURABLE.



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gned to fit most housings, this remarkable new line of y duty rotating anode x-ray tubes incorporate all the of modern technology.

rbly engineered, the Dunlee Duratron 175 and 140 rotating anode have a high heat storage capacity, 175,000 H.U. on the 175 140,000 H.U. on the 140. Their high dissipation rate makes them cable for all types of fluoroscopic, spotfilm and general graphic service.

ially constructed targets (rhenium-tungsten-molybdenum on the tron 175, enlarged solid tungsten on the 140) assure a tube life rpassed in the industry.

ify the x-ray tube insert designed for longer life in today's busy

WARRANTY

Dunlee's Material and Workmanship Warranty accompanying each tube, is our expression of confidence and your assurance of the highest production and inspection standards.

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SQUIBB

a research concept in contrast visualization

for clear definition of disease:

this oral medium is the message...

Oragrafin® Calcium (Squibb Calcium Ipodate) visualizes the gallbladder and ducts quickly and clearly with few undesirable reactions. For rapid or routine studies of the gallbladder and biliary ducts, Oragrafin permits efficient absorption for maximum concentration and excellent contrast—with bowel residue in only a small percentage of patients and few patient problems.

Oragrafin (Squibb Ipodate) in radiography — an advanced medium of biomedical communication. According to McLuhan's[1] provocative new theories of communications, all media are considered "extensions of man"—the means by which he extends his understanding and control of the universe and himself. In biomedical communications, where man monitors the diverse processes of molecular and cellular change, modern contrast radiography is an advanced medium.

Today, in cholangiography and cholecystography, as the medium becomes increasingly oral, the diagnostic message is clear, rapid, and convenient with Oragrafin (Squibb Ipodate).

For summary of contraindications, precautions, and side effects, see end of this advertisement.



the medium:

Oragrafin®

Squibb Ipodate

the message:

maximum concentration... excellent toleration

high absorption index—"No one will dispute the statement that the diagnostic reliability of oral cholecystography depends upon the degree of absorption of the contrast medium employed."[2] Radioisotope studies with ipodate sodium show a markedly improved absorption index (approximately 70 per cent) with no increase in the toxic properties.[2]

excellent opacification—"In addition to its ease of administration and safety, its principal advantages are a high yield of diagnostic films...."[3]

less bowel residue—"Incomplete and variable absorption of a cholecystographic agent is not desirable, for the opacification of the gallbladder is then less dependent on the status of the gallbladder and more a reflection of the percentage absorption."[4]

"Opaque material in the bowel was found in 46 per cent of [105 patients in] the...[iopanoic acid] group as compared with 9 per cent of those [99] of the [Oragrafin Sodium Capsules]...group."[4] In another study, 49 of 100 patients receiving iopanoic acid had residue in the gastrointestinal tract, while only 15 of 100 patients receiving Oragrafin Sodium Capsules had such residue.[5]

no evidence of nephrotoxicity, infrequent side effects—In contrast to findings with other cholecystographic agents, Lewitan and Garcia[6] reported in their 246-patient study: "With ipodate calcium... there was no clinical evidence of immediate or delayed nephrotoxicity in any of the patients given it...."[6] To study possible renal toxicity, "Creatinine clearance tests were also done before and after administration of multiple doses in excess of 6 gm. in 8 cases, and showed no significant alterations."[6] However, "Multiple doses beyond 6 gm. are not recommended."[6]

In their study of 120 patients, Glenn and O'Brien reported "...no reactions in this series of patients attributable to the administration of [Oragrafin]...."[3]

And, McCrory reported that Oragrafin Sodium and Calcium was "...used routinely in cholecystographic studies in approximately 2000 patients with excellent diagnostic films and only rare and mild reactions."[7]

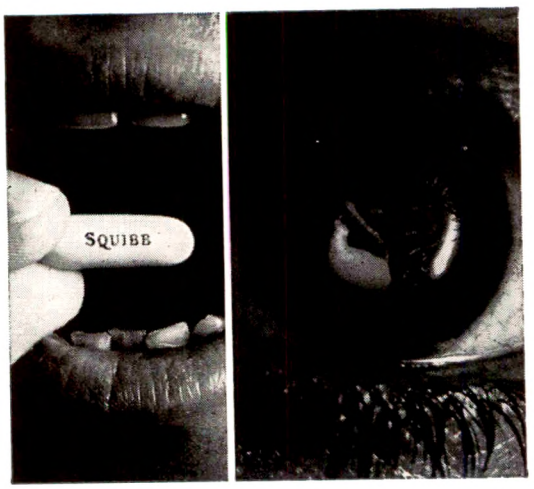
fewer side effects than iopanoic acid—According to White and Fischer,[4] 36 (36.4%) instances of side effects occurred in 99 cases with Oragrafin Sodium, 3 Gm. compared with 87 (82.9%) in 105 cases with iopanoic acid, 3 Gm. Kinds of side effects noted were nausea, vomiting, diarrhea, cramps and dysuria—all less frequent with Oragrafin Sodium (Squibb Sodium Ipodate).

Juhl,[5] in his study of 200 patients (100 on iopanoic acid and 100 on sodium ipodate), found that the incidence of nausea and vomiting was equal in the two groups.[5]

Oragrafin (Squibb Ipodate) dosage schedules
Oragrafin (calcium or sodium ipodate) permits overnight cholecystography and cholangiography.

	Gallbladder Films		Films of the Gallbladder and Biliary Ducts
11 P.M.	6 Capsules OR (or 12 Capsules)	1 packet of Granules (or 2 packets)	6 Capsules (or 1 packet of Granules, if preferred) and
next morning 8 A.M.			1 packet of Granules
9 A.M.	Visualization of gallbladder	Visualization of gallbladder	Visualization of ducts and gallbladder
10 A.M.			
11 A.M.			

For summary of contraindications, precautions, and side effects, see next page.



speed and convenience of Oragrafin® Calcium Granules

Squibb Calcium Ipodate

new clinical study[8] demonstrates improved diagnoses with calcium ipodate—"A group of 114 patients with poorly filled gallbladders after routine administration of iopanoic acid were given 6 gm. of [calcium] ipodate granules immediately following their routine cholecystography. In 66 per cent of these patients opacification of the gallbladders was obtained within 3 hours, allowing a definite diagnosis. Of the remaining 33 per cent, one-half were ultimately proven diseased." "It is apparent that many poorly visualized gallbladders can be rendered visible by the ingestion of ipodate granules.... A whole day may be saved and other diagnostic studies may be performed."[8]

patient convenience—Routine cholecystography night-before procedure is easy for patients to follow; palatable granules further enhance patient acceptability. Rapid clearance of medium permits same-day administration and gallbladder and ductal films, and if necessary, same-day re-examination; reduces need for I.V. studies.

rapid absorption permits same-day re-examination—To determine the cause of nonopacification after routine cholecystography using 6 capsules, physicians may require re-examination by repeating the procedure at a later date (sometimes doubling dose to 12 capsules), or by administering more agent the evening of the first unsuccessful examination (again sometimes doubling dose to 12 capsules), and repeating the study the next day. "The advantage of the calcium ipodate method is that the examination can be completed in five additional hours with a limited dose of contrast agent."[9]

"a valuable medium for peroral cholegraphy"[6]—Rapidly absorbed from the gastrointestinal tract, calcium ipodate has been reported by some investigators to be diagnostically superior to other oral cholangiographic contrast agents.[10,11] With careful timing of the examination and the use of tomograms or laminograms, the frequency of good results can approximate that obtained with intravenously administered agents.[10] According to Lewitan and Garcia,[6] the medium's relative safety makes it a valuable medium for peroral cholegraphy. Timesaving and economical Oragrafin Calcium Granules may be particularly useful in certain patients for whom I.V. radiography presents potential hazards, such as elderly patients and those with cardiovascular disease.

Unique among oral media, Oragrafin Calcium Granules permits same-day films of the gallbladder and the ductal system.

dosage schedule for films of gallbladder and ductal system

8 A.M.	2 packets of granules
9 A.M.	visualization of ducts
10 to 11 A.M.	visualization of gallbladder

Contraindications: Contraindicated for persons sensitive to oral iodine compounds or for patients with *combined* renal and hepatic disease or *severe* kidney impairment. Gastrointestinal disorders, which may interfere with absorption, or liver dysfunction, which may result in inadequate biliary secretion of medium, are likely to result in unsatisfactory visualization.

Precautions and Side Effects: Mild and transient nausea, vomiting, or diarrhea sometimes occur; but the incidence can be reduced by using the calcium granules and restricting the dosage to 3 Gm. Transient headache, dysuria, or abdominal pains may occur.

Hypersensitivity reactions may include urticaria, serum sickness-like reactions, and rarely anaphylactoid shock. They are more likely to occur in the individual with a history of allergy, asthma, hay fever, or urticaria and in the individual who is known to be hypersensitive to iodine compounds. Antihistamines and corticosteroids are used to control hypersensitivity reactions; but the occasional serious anaphylactoid reactions require the immediate use of epinephrine or phenylephrine, oxygen, and intravenous corticosteroids.

For full information see Package Insert.

Supply: The calcium salt (Oragrafin Calcium Granules) is available in single-dose foil packets providing 3 Gm. of calcium ipodate as Granules dispersed in flavored sucrose. The sodium salt is available in capsule form (Oragrafin Sodium Capsules) providing 0.5 Gm. sodium ipodate per capsule.

References: 1. McLuhan, M.: Understanding Media: The Extensions of Man, New York, McGraw-Hill Book Company, 1966. **2.** Sanen, F. J.: Amer. J. Roentgen. *88*:797 (Oct.) 1962. **3.** Glenn, J. C., Jr., and O'Brien, P. S.: Southern Med. J. *56*:167 (Feb.) 1963. **4.** White, W. W., and Fischer, H. W.: Amer. J. Roentgen. *87*:745 (April) 1962. **5.** Juhl, J. H., *et al.*: Radiology *80*:87 (Jan.) 1963. **6.** Lewitan, A., and Garcia, J. F.: Amer. J. Dig. Dis. *10*:219 (March) 1965. **7.** McCrory, E.: J. Tenn. Med. Ass. *58*:258 (Aug.) 1965. **8.** Root, H.: Amer. J. Roentgen. *101*: 621 (Nov.) 1967. **9.** Crummy, A. B.: Wisconsin Med. J. *65*:84 (Feb.) 1966. **10.** Saltzman, G. F.: Acta Radiol. *54*: 417, 1960. **11.** Ludin, H., and Lauchenauer, C.: Schweiz. Med. Wochenschr. *90*:471, 1960.

for clear definition of disease: in oral cholangiography and cholecystography

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identifying number is fed into the keyboard. Searches up to 1558 folders per second.

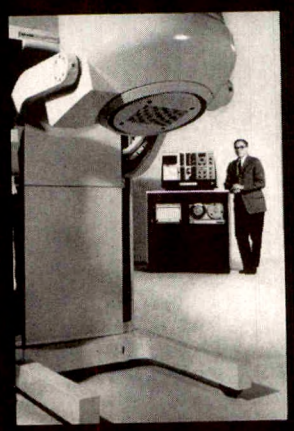
Monotrieve, for "medium to low activity" films, codes storage cradle openings rather than individual files. Cradles are stored in face-to-face linear banks arranged as high or as long as space permits. Real space economy. Cradles are scanned, 50 inches per second, then brought by keyboard command to the operator. No walking, reaching or stooping.

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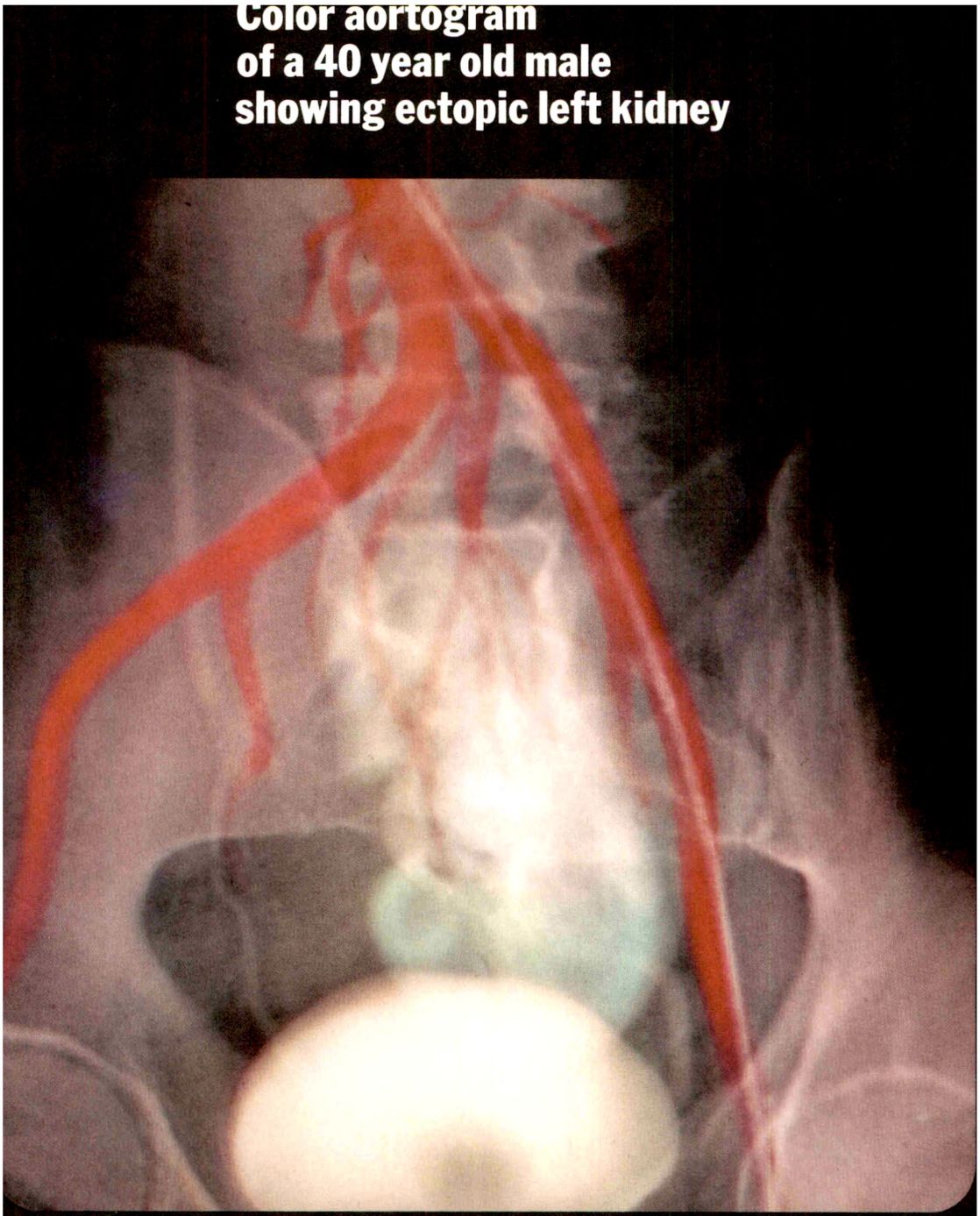
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renal abnormalities in color
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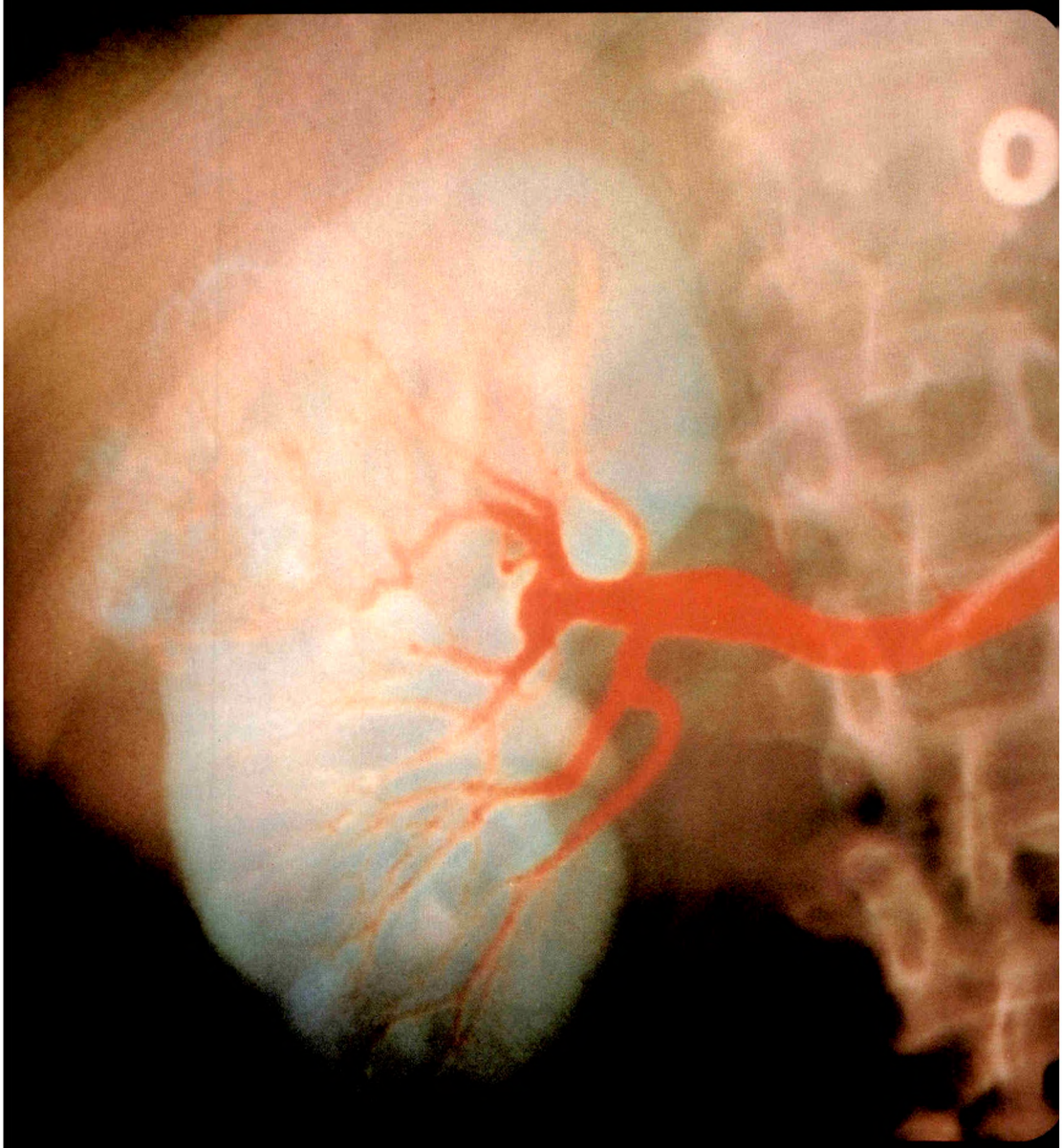
Color aortogram of a 40 year old male showing ectopic left kidney



he color films were prepared by a special technique by Robert L. Wise, M.D. of the Lahey Clinic
oundation and New England Baptist Hospital, Boston, Mass.

ypaque® sodium 50% (brand of sodium diatrizoate) is a versatile aid in the diagnosis of a
ide variety of kidney conditions. Because of the fine detail obtained, **Hypaque® sodium 50%**
elps delineate masses, cysts, vascular disorders, and anomalies or malformations of the kidney.

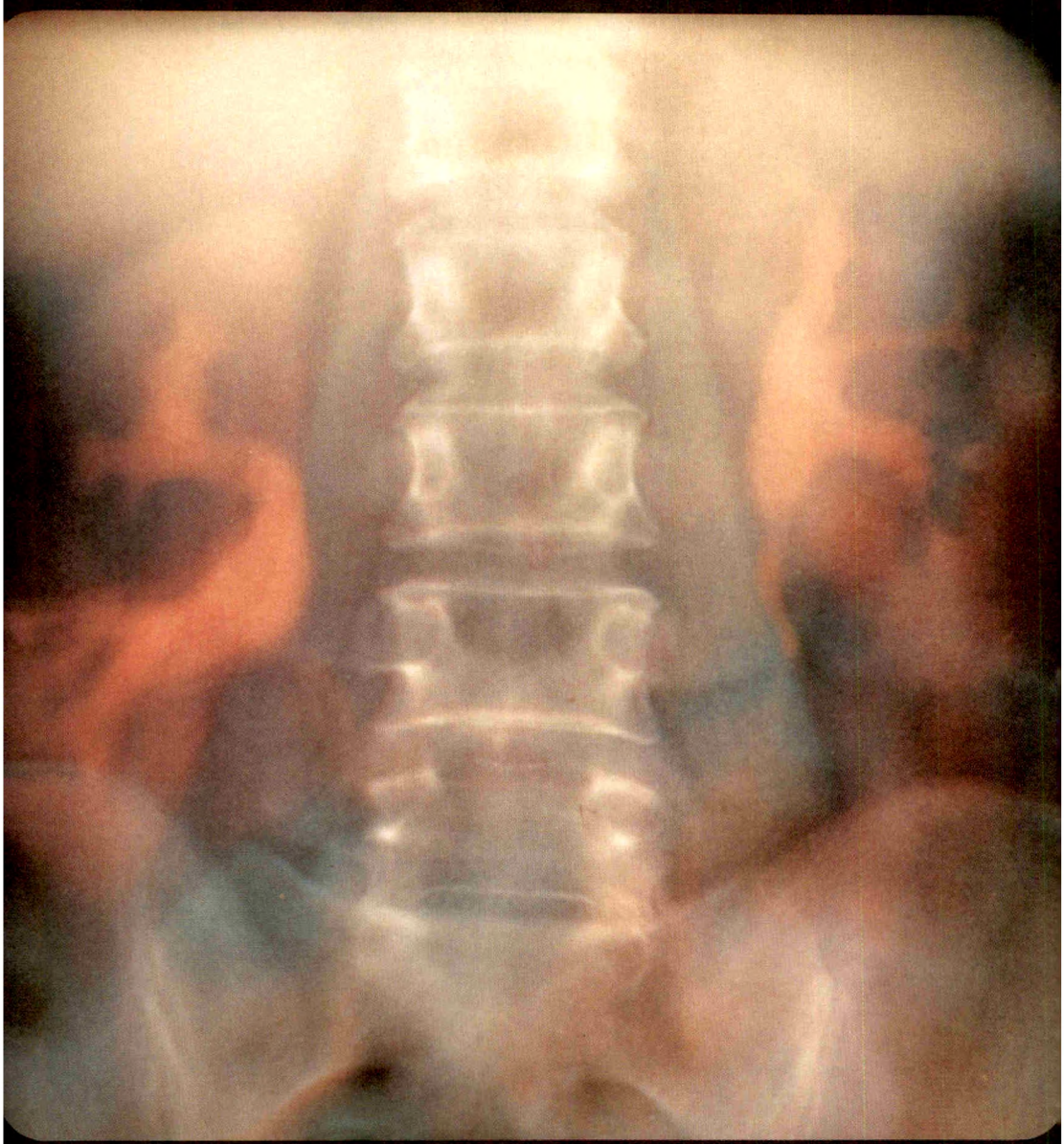
Color selective renal arteriogram of a 56 year old man showing adenocarcinoma of the kidney



ypaque® sodium 50% (brand of sodium diatrizoate) provides the *precise anatomic informa*
on required for diagnosing suspected parenchymal diseases of the kidney.

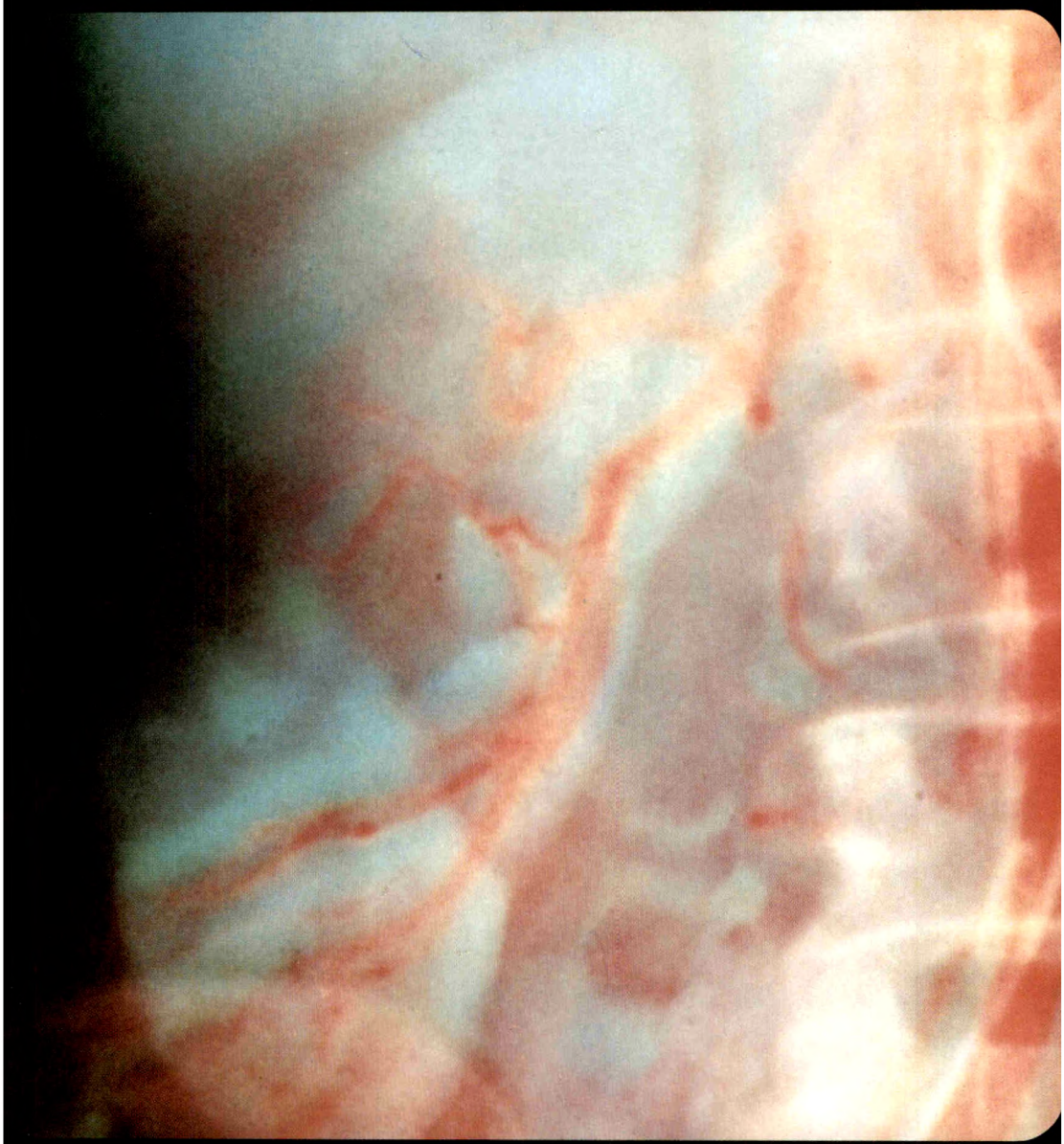
Because **Hypaque® sodium 50%** has the *lowest viscosity* of *all* media for aortography an
lective renal arteriography, the radiologist will find administration by needle or catheter easier

Color Drip Infusion Urogram of a 64 year old female suggesting large cyst, right kidney



Using 300 ml. Hypaque® sodium in a 25% concentration, the radiologist can obtain valuabl
evidence in cases of renal abnormalities such as agenesis, duplication, ectopia, neoplasm or cys
When indicated, subsequent arteriography with **Hypaque® sodium 50% (brand of sodium dia**
rizoate) will opacify the entire renovascular s tem for confirmation or for additional informatio

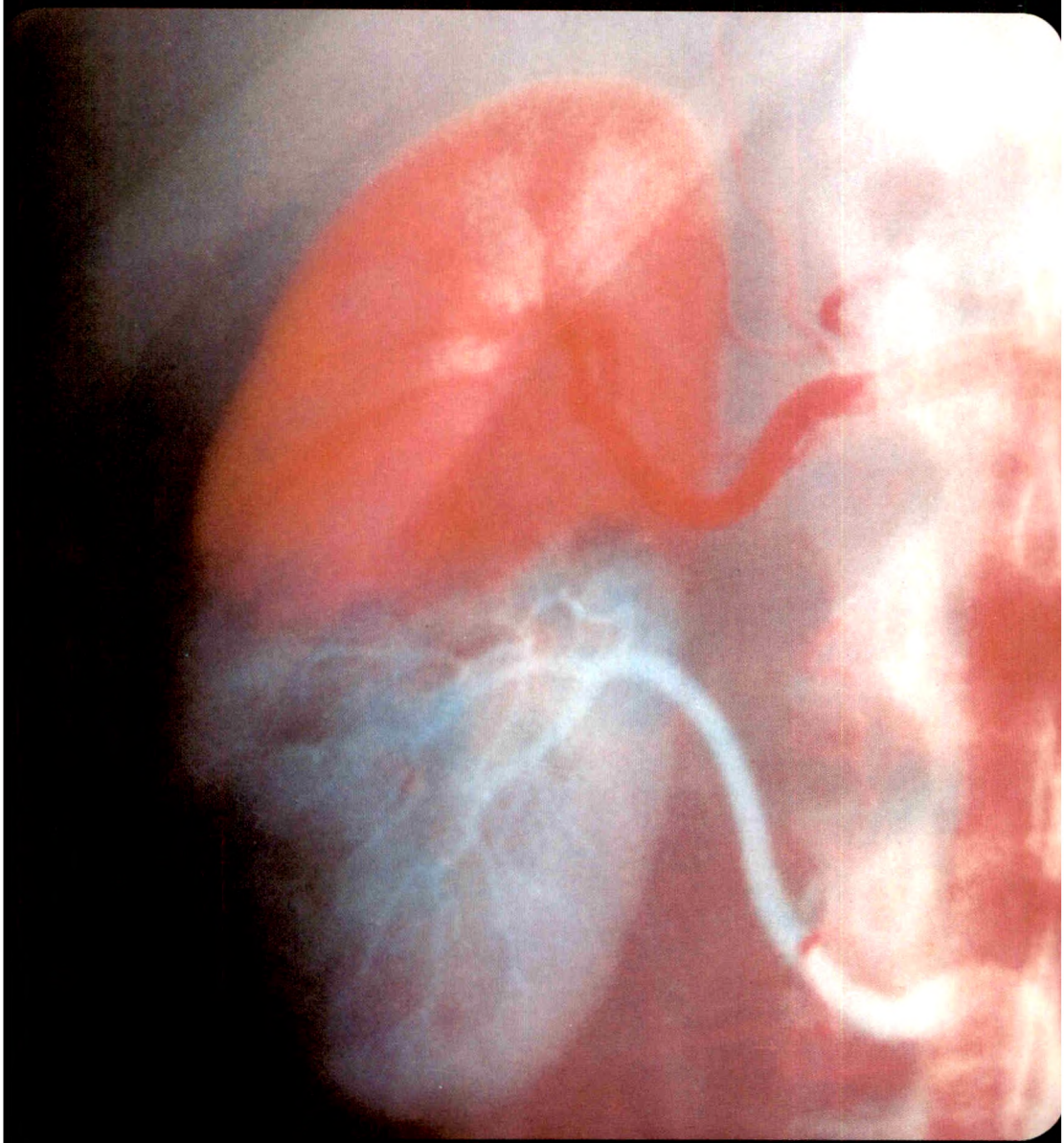
Abdominal Aortogram of same patient, confirming presence of right renal cyst



ypaque® sodium 50% (brand of sodium diatrizoate) provides information helpful in *differ ntiating between a renal cyst and neoplasm*—often a difficult diagnostic problem.

However, should a tumor be involved, **Hypaque® sodium 50%** provides detailed informatio egarding *size, extension,* and *vascular supply.*

Color aortogram of a 38 year old male showing dual renal blood supply on the right



lypaque® sodium 50% (brand of sodium diatrizoate) has optimal iodine content (300 mg/ml nd the advantage of low viscosity for accurate diagnosis and evaluation of major arteries i he kidney.

Angiography with **Hypaque® sodium 50%** helps supply valuable diagnostic information i lemonstrating aneurysmal change or degree of patency of an arteriosclerotic vessel. It also aid he surgeon in determining if a stenotic vessel may be responsible for life-threatening hyper ension.

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sodium

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The versatile contrast agent for definitive renal visualization

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Summary of Full Prescribing Information

Hypaque® Sodium 50% brand of **sodium diatrizoate** Sterile Aqueous Injection (Weight/Volume)

Excretory Urography and Drip Infusion Pyelography

Description: Hypaque sodium is sodium 3,5-diacetamido-2,4,6-triidobenzoate, a radiopaque medium used to delineate internal structures.

Warning: Do not use Hypaque sodium for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

General and Specific Precautions: Caution is advised in patients with a history of bronchial asthma, other allergic manifestations, or of sensitivity to iodine; these conditions represent a special risk, though not an absolute contraindication. To avoid or minimize possible allergic reactions, premedication with antihistamines may be considered. Benadryl (diphenhydramine hydrochloride) in the same syringe with Hypaque may result in precipitation. A test dose of contrast medium is not entirely reliable. Severe reactions, including fatalities, have occurred with a test dose as well as with the full diagnostic dose.

Caution is advised in patients with severe cardiovascular disease. In patients with impaired renal function and cardiovascular disease, drip infusion pyelography imposes a sudden osmotic and sodium load which can precipitate congestive heart failure. Contrast media injected into arteries or veins can promote sickling of red cells in susceptible individuals. In patients with reduced renal function, repeat of excretory or retrograde pyelography should be delayed at least 48 hours to avoid temporary suppression of urine. In preparation for excretory urography of patients with multiple myeloma, partial dehydration is not recommended, since this may predispose to the precipitation of myeloma protein in the kidney tubules. When thyroid function studies (PBI and 24-hour radioiodine uptake levels) are indicated, they should be performed *prior* to radiographic studies or several days afterwards, to avoid inaccurate results.

Hypaque sodium 50% should always be injected at body temperature.

General and Specific Adverse Reactions: Adverse reactions, usually of a minor nature, have occurred in 10-14 per cent of patients who have received Hypaque intravenously. Reactions due to *faulty technique* include hematomas and ecchymoses, following extravasation from the vein, and pyrogenic reactions. *Hemodynamic reactions* include vasodilatation with flushing, hypotension and, rarely, vein cramp or thrombophlebitis. Serious *cardiovascular reactions* include rare cases of cardiac arrhythmias (e.g., ventricular fibrillation), shock, and cardiac arrest. Transient proteinuria may occur occasionally following the injection of radiopaques and, rarely, oliguria and anuria have been reported secondary to a hypotensive reaction. *Allergic reactions* include asthmatic attacks, nasal and conjunctival symptoms, cutaneous reactions such as urticaria and, rarely, anaphylactic shock, sometimes with fatal outcome. Severe reactions may also be manifested by signs and symptoms relating to the *respiratory system* (dyspnea, cyanosis, pulmonary or laryngeal edema), or to the *nervous system* (restlessness, confusion, or convulsions). *Other reactions* include nausea, vomiting, excessive salivation, anxiety, headache, and dizziness. Infrequently, "iodism" (salivary gland swelling) from organic compounds appears two days after exposure and subsides by the sixth day. Reactions to drip infusion pyelography may not appear until some hours after the examination.

Angiography (Peripheral Arteriography and Venography)

Precautions *(See also General Precautions):* Extreme caution is advised in considering peripheral arteriography in patients suspected of having thromboangiitis obliterans (Buerger's disease). Any procedure (even needling or insertion of a catheter) may induce a severe arterial and/or venous spasm. Caution is also advisable in patients with severe ischemia associated with ascending infection.

Adverse Reactions *(See also General Adverse Reactions):* In addition to those listed under General Adverse Reactions, are those due to arterial trauma during the procedure (i.e., needling, insertion of catheter, subintimal injection, perforation, etc.) as well as to the hypertonicity or effect of the medium; also reported are transient arterial spasm, extravasation, hemorrhage, hematoma with tamponade, injury to nerves proximal to artery, thrombosis (rare in venography, if vein is irrigated following injection), dissecting aneurysm, arteriovenous fistula, (e.g., with accidental perforation of femoral artery and vein during needling) transient leg pain from contraction of calf muscles in femoral arteriography; transient hypotension after intraarterial (brachial) injection, and brachial plexus injury with axillary artery injections.

Cerebral Angiography: Because of the special techniques required, it is recommended that Hypaque sodium be used for this purpose only by persons skilled and experienced in carrying out this procedure.

Contraindication: Carotid angiography should be avoided during the progressive period of a stroke, since this increases the risk of cerebral complications.

Precautions *(See also General Precautions):* Select patients for this procedure with care. Use the 50 per cent solution with caution in extreme senility (but not old age, *per se*), advanced arteriosclerosis, severe hypertension, and cardiac decompensation.

The diagnostic value of the procedure, according to many authorities, when employed early enough in locating lesions amenable to surgery, may outweigh the added risk to patients who have recently experienced cerebral embolism or thrombosis (stroke syndrome). A small number of postangiographic fatalities, including progressive thrombosis, have occurred in which the procedure did not appear to play a role. Patients with severe cerebrovascular disease may be examined primarily by indirect methods of angiography.

Care should be exercised to avoid contaminating catheters, syringes, needles, and contrast media with glove powder or cotton fibers.

Angiography is hazardous in subarachnoid hemorrhage. In migraine, the procedure can be hazardous because of ischemic complications, particularly if performed during or soon after an attack.

Adverse Reactions *(See also General Adverse Reactions):* The major sources of complications are faulty technique, occlusive atherosclerotic vascular disease, repeated injections of the contrast media, and higher doses than those recommended.

Untoward reactions are mostly mild and transient, although permanent visual field defects and deaths have been reported.

Vascular reactions: flushing, vessel spasm, thrombophlebitis, and cutaneous petechiae.

Neurologic complications: transient cerebral blindness, neuromuscular disorders, convulsions, coma, hemiparesis, unilateral dysesthesias, visual field defects, aphasia, and respiratory difficulties.

Aortography

Precautions *(See also General Precautions):* Special caution is advised to avoid inadvertent intrathecal injection when using the translumbar technique. The incidence and severity of reactions or complications that may occur are influenced by: the care and experience with which the procedure is performed; the amount and type of medium used; the age and condition of the patient; and the premedication and anesthesia used. Since aortography is not without some danger, it should be performed only by those experienced in the technique. Wherever possible, repeated injections of the solution during a single study should be avoided.

Adverse Reactions *(See also General Adverse Reactions):* Renal damage and shutdown; neurologic complications such as transverse myelitis or paraplegia; cardiovascular complications such as shock, cardiac arrest or failure, coronary occlusion, arterial thrombosis, embolism, and perforation of vessels; extravasation or hemorrhage from the puncture site or retroperitoneal catheter perforation; necrosis of the intestinal wall; acute pancreatitis; deaths; diffuse cutaneous petechiae; subintimal injection and aortic dissection.

Intraosseous Venography

See General Precautions and Adverse Reactions. A general anesthetic is sometimes necessary since the method is painful. Occasionally, extravasation of the contrast medium from the needle into the soft tissue may occur.

Direct Cholangiography

Precaution *(See also General Precautions):* This procedure should be used with caution in the presence of acute pancreatitis, injecting no more than 5 to 10 ml. without undue pressure.

Adverse Reactions *(See also General Adverse Reactions):* These may be attributed to injection pressure or excessive volume of the medium, resulting in overdistention. Such pressure may produce a sensation of epigastric fullness, followed by moderate pain in the back or right upper abdominal quadrant, which will subside when injection is stopped.

Some of the medium may enter the pancreatic duct and cause a transient serum amylase elevation 6 to 18 hours later, without apparent ill effects. Pancholangitis resulting in liver abscess has been reported. Occasionally, nausea, vomiting, fever, and tachycardia have been observed.

Hysterosalpingography

Contraindications: Menstruation, active or imminent; infection in any part of the genital tract, including the external genitalia; pregnancy, known or suspected. Use not advised for six months after end of pregnancy, or 30 days after conization or curettement.

Precaution *(See also General Precautions):* Caution should be exercised in patients with known or suspected carcinoma to avoid possible spread of the lesion by the procedure.

Splenoportography

Precautions *(See also General Precautions):* Procedure should be performed with caution on patients with blood dyscrasias, a tendency to severe bleeding, or a spleen recently become tender and palpable.

Adverse Reactions *(See also General Adverse Reactions):* Persistent hemorrhage with hemoperitoneum has been reported, and, in some instances, hemorrhage has required splenectomy.

How Supplied: Ampuls of 30 ml., boxes of 1, 10, and 25. A 1 ml. sensitivity test ampul is furnished with each ampul. Vials of 20 and 30 ml., rubber stoppered, boxes of 1, 10, and 25. Vials of 50 ml., rubber stoppered, boxes of 1 and 10. Each vial contains sufficient excess to permit withdrawal of 1 ml. for testing sensitivity.

If the solution is chilled, crystals may form but will readily dissolve if the ampul or vial is placed in moderately hot water before use. Cool to body temperature before injecting.

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EXPERIMENTAL STUDIES OF THE SPLANCHNIC CIRCULATION OF THE RABBIT AFTER LIGATION OF THE SUPERIOR MESENTERIC ARTERY*

I: ANGIOGRAPHIC AND PHYSIOLOGIC STUDIES

By FREDERICK J. BONTE, M.D., GEORGE C. CURRY, M.D.,†
and ROBERT W. PARKEY, M.D.
DALLAS, TEXAS

BOWEL ischemia and necrosis caused by impairment of mesenteric arterial blood flow remains a very serious medical problem, for clinical diagnosis is difficult and the underlying mechanisms of the disorder are still not completely understood despite extensive research by many competent investigators. For example, bowel infarction often develops after occlusion of the superior mesenteric artery or one of its branches, but not always. It is also possible for bowel to become irreversibly ischemic without any demonstrable arterial or venous obstruction. Infarction due to vascular occlusion lends itself to surgical correction, but infarction without occlusion is an almost uniformly fatal condition regardless of the course of management, and a surgical approach to it is probably contraindicated. Therefore, the managing clinician must not only suspect bowel infarction as the cause of symptoms in his patient, but must know whether he is dealing with occlusive or nonocclusive mesenteric arterial disease. Obviously, selective roentgen arteriography will answer some of these questions, but this itself is a rather rigorous procedure and a simpler test is required to select those patients in whom arteriography might be indicated.

We decided to investigate, in the laboratory, some of the mysteries of abnormal splanchnic blood flow and chose the rabbit as our experimental animal because of certain fundamental similarities between its splanchnic vasculature and that of man.

MATERIALS AND METHODS

ANGIOGRAPHIC STUDY AND SURVIVAL OF RABBITS AFTER LIGATION OF THE SUPERIOR MESENTERIC ARTERY

Each of 30 healthy albino male rabbits, weighing between 2 and 3 kg., was anesthetized by the intravenous administration

* Presented at the Sixty-ninth Annual Meeting of the American Roentgen Ray Society, New Orleans, Louisiana, October 1–4, 1968.
From the Department of Radiology, The University of Texas Southwestern Medical School at Dallas, and Parkland Memorial Hospital, Dallas, Texas.
This work was supported in part by Grant HE-05181 from the National Institutes of Health, USPHS, and in part by a grant from the Southwestern Medical Foundation, Dallas, Texas.
† Clinical Fellow of the American Cancer Society, Inc.

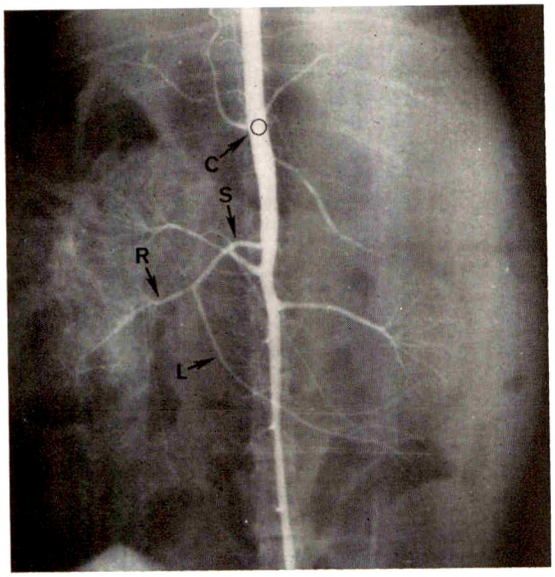


FIG. 1. Anteroposterior aortogram of rabbit made immediately after injection shows the superior mesenteric artery (S) and its ileocecocolic (R) and left (L) branches. C is the origin of the celiac axis.

of 30 mg. of nembutal per kg. of body weight. Supplemental maintenance doses of nembutal were administered thereafter as required. A single end-hole catheter was introduced retrograde into the abdominal aorta through the femoral artery and positioned so that the tip of the catheter lay above the origin of the celiac axis. Through a midline abdominal incision the origin of the superior mesenteric artery from the abdominal aorta was exposed, doubly ligated and cut. The abdomen was then closed.

Aortography was performed by injection of 4 ml. of sodium iothalamate 66.8 per cent (conray 400). The bolus was delivered in 0.5 second with a Viamonte-Hobbs injector. Films were exposed in a roll film changer at a rate of 2 films per second for a total of at least 18 seconds. The first aortography performed on each rabbit was a control study, made before ligation of the superior mesenteric artery. The next aortograms were obtained from 1 to 14 minutes after interruption of the superior mesenteric artery, and subsequent contrast studies were obtained at 1 to 2 hour intervals until the animal died.

Six animals were used as surgical controls for this group. They underwent superior mesenteric artery ligation but aortography was not done. These animals were observed under anesthesia until death.

Four additional rabbits (aortographic controls) were subjected to aortography in approximately the same time sequence as the study group above, but the superior mesenteric arteries were not interrupted. These animals were observed, under anesthesia, for 11 hours, and none showed signs of distress at the end of this period. All 4 rabbits survived.

EFFECT OF HEPARINIZATION ON SURVIVAL AFTER LIGATION

In order to determine whether or not clotting of blood in superior mesenteric and collateral vessels contributed to early demise, 5 rabbits were subjected to superior mesenteric artery ligation and were catheterized for aortography as described above. Each of the animals in this group was given 1,000 units of heparin intravenously immediately after obstruction of the superior mesenteric artery. Arteriographic patterns were determined at the intervals described above. Each animal was observed, under anesthesia, until it died.

Five additional animals were subjected to the same anesthesia and surgical procedures and were also given 1,000 units of heparin intravenously, but arteriography was not done. Survival times were also recorded for this group.

Five control rabbits received heparin and were observed under anesthesia for 11 hours.

STUDY OF POSSIBLE SUPERIOR MESENTERIC ARTERY-PORTAL VEIN SHUNTING FOLLOWING LIGATION

The studies described above had introduced the possibility of shunting of opacified arterial blood from the superior mesenteric artery to the portal vein after superior mesenteric artery ligation. In order to test this possibility, each of a group of 5 rabbits was anesthetized and the portal vein was exposed through a right subcostal incision. Blood samples were obtained from the por-

tal vein proximal to the entry of the splenic vein by direct needle puncture before, and at various intervals after, ligation of the superior mesenteric artery. Blood oxygen saturations were measured with an A–O Oximeter model 10800.

RESULTS

ANGIOGRAPHIC STUDY AND SURVIVAL OF RABBITS AFTER LIGATION OF THE SUPERIOR MESENTERIC ARTERY

Most of the blood supply to the small and large intestine of the rabbit is derived from the superior mesenteric artery (S, Fig. 1). The largest branch is the ileocecocolic artery (R) which approximates in size the superior mesenteric trunk, and is distributed to the terminal ileum, cecum and ascending colon. The rabbit cecum and ascending colon are relatively larger than are these structures in man. Beyond the origin of the ileocecocolic artery, about 20 intestinal arteries arise from the left branch (L) of the superior mesenteric artery and are distributed to the small intestine.

As in man, the 3 major branches of the celiac trunk (C, Fig. 1) are the splenic, left gastric and hepatic arteries. The inferior mesenteric artery is small and supplies the descending colon.

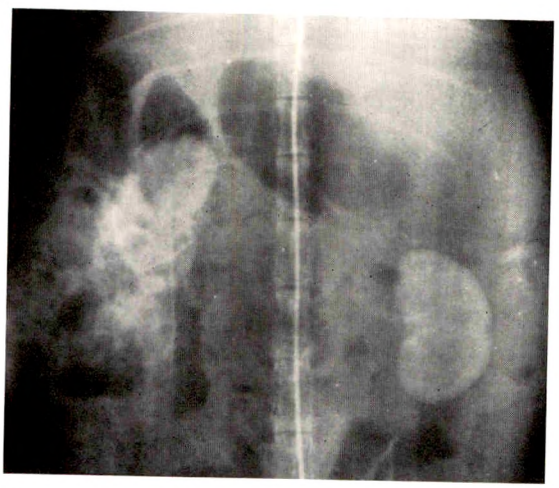


Fig. 2. Venous phase of aortogram seen in Figure 1. The study was made 18 seconds after injection of contrast material. Note that there is no demonstrable opacification of the mesenteric or portal veins.

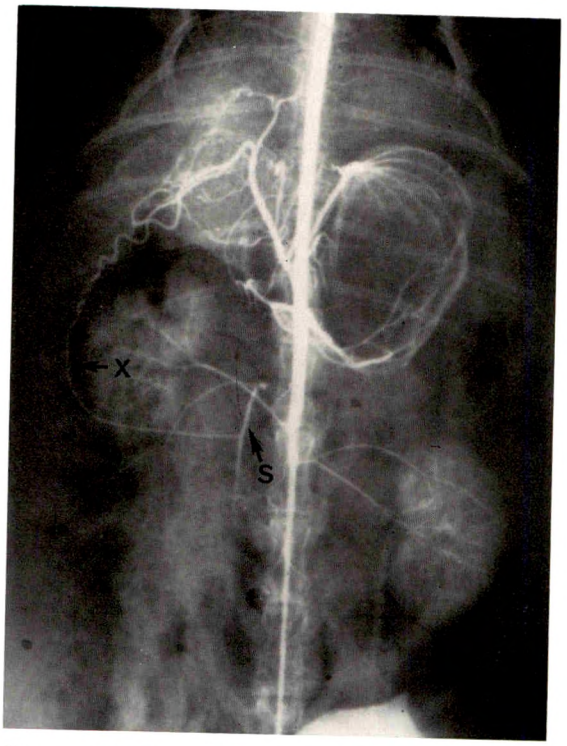


Fig. 3. Anteroposterior aortogram made 6 seconds after injection and 6 hours after ligation of the superior mesenteric artery. Note the tortuous collateral artery (X) filling from one of the branches of the celiac axis and entering the superior mesenteric artery (S) distal to the point of ligation.

Figure 2 represents the venous phase of the normal arteriogram seen in Figure 1. Note that the portal and mesenteric veins are not opacified.

Following occlusion of the superior mesenteric artery, postoperative aortography showed some degree of delayed opacification of the ligated artery through collateral channels in almost all animals (Fig. 3). At least the proximal portion of the obstructed superior mesenteric artery was easily identified in most, and in about half of the animals relatively good filling was obtained by visible collateral flow through a prominent vessel originating from the celiac axis (X, Fig. 3). That collateral flow is quickly established was demonstrated by its presence in several animals on aortograms made within 30 seconds after ligation.

Regardless of the extent of collateral replacement of the obstructed arterial flow,

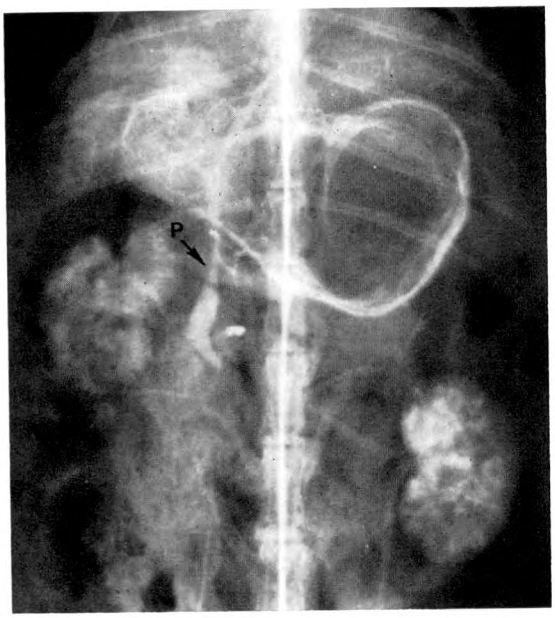


FIG. 4. Anteroposterior aortogram of rabbit 6 hours after ligation of the superior mesenteric artery. Study was made 15 seconds after injection and shows densely opacified portal vein (P).

serial aortograms made at intervals after ligation always showed a progressive decrease in arterial opacification, and in those made shortly before the death of each animal there was usually little or no evidence of arterial blood flow, as is shown in Figure 6. Figure 6*A* is an aortogram from a series made 1 minute after ligation and shows the establishment of collateral flow (R, L). The study in Figure 6*B* was made 7 hours and that in Figure 6*C* 10 hours after ligation, and they illustrate progressive diminution of flow in the obstructed superior mesenteric artery.

Some time later, following occlusion of the superior mesenteric artery in all animals, almost all aortograms demonstrated better visualization of the portal venous system than was seen in the preligation studies. In fact, aortograms made late after ligation often showed an opacified portal vein when there had been little or no evidence of opacification of the mesenteric artery or its branches. Figures 4 and 5 demonstrate examples of postligation opacification of the portal vein (P). In several animals it was even possible to outline the distribution of some of the finer radicals of the superior mesenteric vein (M, Fig. 5). Also, in Figure

TABLE I

SURVIVAL OF RABBITS AFTER LIGATION OF THE SUPERIOR MESENTERIC ARTERY*

	No.	Mean Survival	Range
Aortographic control	4	All survived	
Surgical control	6	9.9 hr.	6.2–12.7 hr.
Experimental group	30	7.8 hr.	4.0–13.75 hr.

* The surgical control and experimental groups were observed under intravenous nembutal anesthesia until death, and the aortographic controls were observed under anesthesia for 11 hours. The experimental group had ligation of the superior mesenteric artery and frequent aortographies. The surgical control group had ligation of the superior mesenteric artery, but no aortographies. The aortographic control animals had repeated aortography, but the superior mesenteric arteries were not ligated.

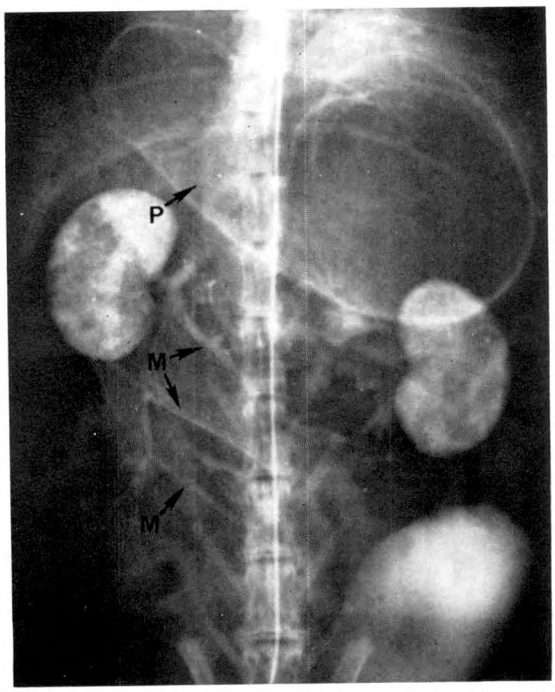


FIG. 5. Anteroposterior aortogram of a rabbit made 30 minutes after ligation of the superior mesenteric artery. Study, made 17 seconds after injection, shows opacified portal vein (P) and opacified branching mesenteric veins (M). The shadows of opacified branches of the superior mesenteric artery are seen superimposed upon, and lying within, the shadows of the opacified veins.

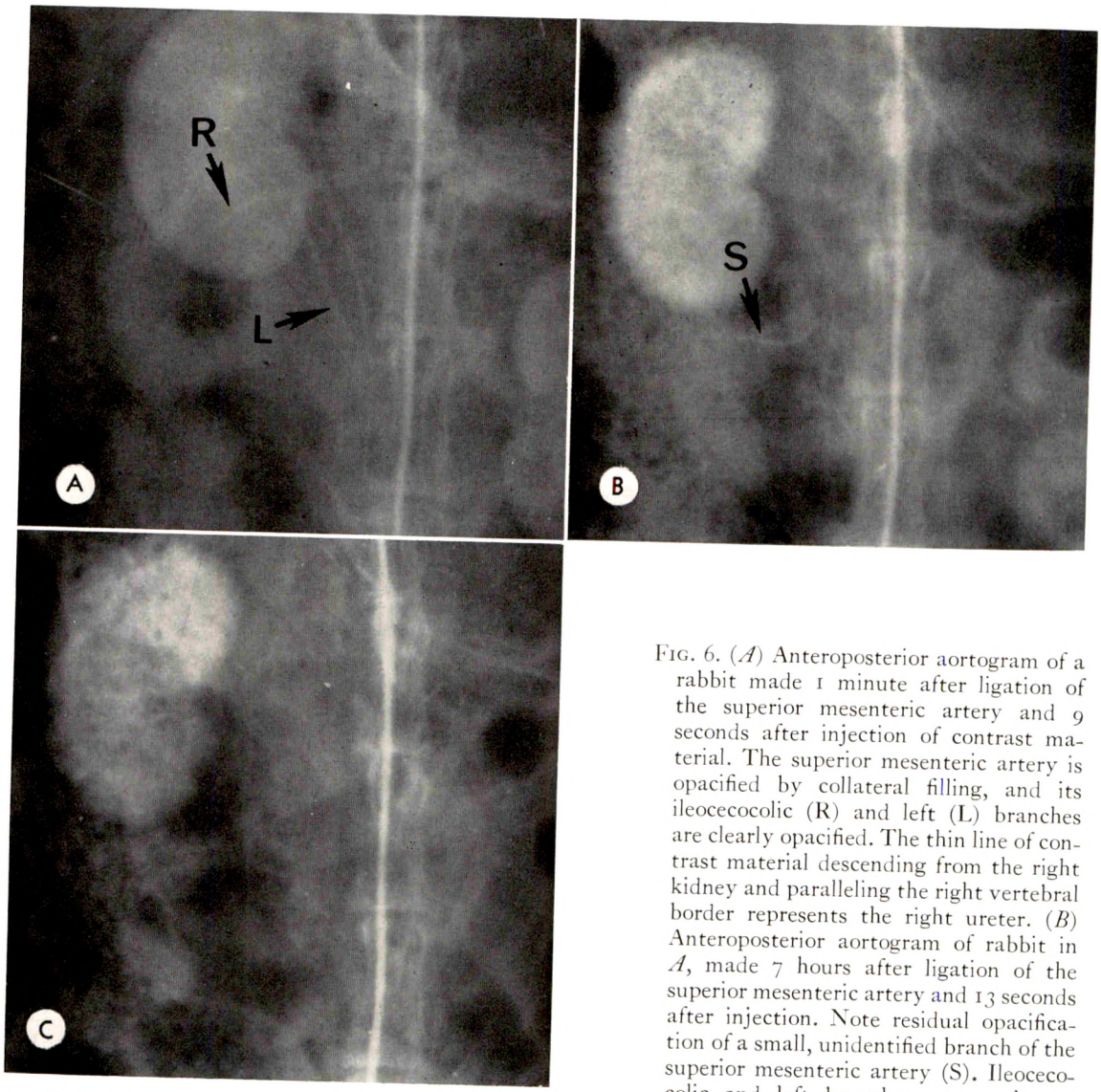


Fig. 6. (*A*) Anteroposterior aortogram of a rabbit made 1 minute after ligation of the superior mesenteric artery and 9 seconds after injection of contrast material. The superior mesenteric artery is opacified by collateral filling, and its ileocecocolic (R) and left (L) branches are clearly opacified. The thin line of contrast material descending from the right kidney and paralleling the right vertebral border represents the right ureter. (*B*) Anteroposterior aortogram of rabbit in *A*, made 7 hours after ligation of the superior mesenteric artery and 13 seconds after injection. Note residual opacification of a small, unidentified branch of the superior mesenteric artery (S). Ileocecocolic and left branches are no longer opacified. Opacification of the right ureter is again noted. (*C*) Anteroposterior aortogram of rabbit in *A* and *B* made 10 hours after ligation of the superior mesenteric artery and 16 seconds after injection. Note that there is no longer any evidence of opacification of the superior mesenteric artery and its branches.

5, the collaterally filled branches of the superior mesenteric artery are seen superimposed upon the opacified vein. It should be noted that portal vein opacification did not occur after repeated injection of contrast material in the aortographic control group (Table 1).

Mean postligation survival time in the study group of 30 rabbits was 7.8 hours, with a range of from 4.0 hours to 13.75 hours (Table 1). The control group of animals with ligation but without aortography showed a mean survival time of 9.9 hours (Table 1), with a range of from 6.2 to 12.7 hours. Under the conditions of this experiment, there is probably no significant difference in these survival times. It was not possible to predict survival on the basis of angiographic observation; *i.e.*, the degree of arterial or venous opacification after

TABLE II

SURVIVAL OF RABBITS IN HEPARIN EXPERIMENT*

	No.	Mean Survival	Range
Control	5	All survived	
Experimental (heparin +aortography)	4	9.3 hr.	6.0–11.7 hr.
Experimental (heparin; no aortography)	5	8.3 hr.	7.0–10.0 hr.

* The first experimental group had ligation of the superior mesenteric artery, was heparinized and had frequent aortographies. The second experimental group had ligation of the superior mesenteric artery and heparin but had no aortographies. Both experimental groups were observed, under anesthesia, until death. The control group received intravenous nembutal anesthesia and heparin but had no aortographies, and the superior mesenteric artery was not ligated.

ligation of the artery bore no constant relationship to postoperative survival time.

EFFECT OF HEPARINIZATION ON SURVIVAL AFTER LIGATION

As we have mentioned above, serial aortograms made after ligation revealed a gradually decreasing volume of arterial flow, sometimes to the point of there being no further opacification of the ligated artery (Fig. 6, *A*, *B* and *C*). One possible explanation was the occurrence of clotting in collateral channels or in the distal branches of the ligated artery, so that the heparin studies described above were done.

No change in the sequence of arteriographic events was detected in the 4 heparinized animals which had serial aortography. Mean survival times in this group and in the 5 heparinized animals observed without aortography were similar (Table II). The survival times of the entire series of heparin-treated animals approximated those of the nonheparinized series (Tables I and II), suggesting that clotting was not of primary importance in death from bowel ischemia.

STUDY OF POSSIBLE SUPERIOR MESENTERIC ARTERY-PORTAL VEIN SHUNTING FOLLOWING LIGATION

When the recurring pattern of increased portal and mesenteric venous opacification after ligation became apparent, efforts were made to explain this observation. The possibility of backflow from the nonoccluded splenic, gastric or inferior mesenteric circulation was considered. That there is still a forward flow in the portal system after ligation of the superior mesenteric artery was shown by the fact that serial filming following injection of contrast material into a branch of the superior mesenteric vein after arterial occlusion demonstrated a normal direction of flow in the portal system.

That portal vein opacification is not merely the result of the cumulative effect of repeated injections of contrast material is shown by the fact that those rabbits subjected to repeated aortography (aortographic controls, Table I) demonstrated no increase in opacification of the portal system. The study in Figure 5, with intense opacity of the portal vein and its branches, represents only the second injection of contrast material in this rabbit.

A logical explanation seemed to be the opening of multiple arteriovenous shunts in the ligated system, allowing the relatively rapid passage of undiluted contrast material into the venous side. To test this hypothesis we measured oxygen saturation in portal venous blood before, and at intervals up to 120 minutes after, ligation of the superior mesenteric artery in 6 rabbits (Table III). Note that oxygen saturation of blood in the proximal portal vein rose in 5 of the 6 animals within 30 minutes after

TABLE III

PER CENT OXYGEN SATURATION OF PORTAL VENOUS BLOOD SAMPLES*

Animal	Preligation	Postligation (min.) 30	60	120
1	70	80	65	64
2	65	69	69	58
3	64	70	72	65
4	72	65	—	61
5	62	72	—	54
6	64	69	—	57

* These were obtained from each of the 6 rabbits before, and at 30, 60 and 120 minutes after ligation of the superior mesenteric artery.

ligation, and fell in only 1 (4, Table III). Thereafter, there was a tendency toward decrease in portal venous blood oxygen saturation which was well established in 5 of the 6 animals within 120 minutes of ligation.

DISCUSSION

The choice of the rabbit as an experimental animal was based on the similarity of its splanchnic vasculature to that of man. The arcuate system of the rabbit's mesenteric circulation lacks the complexity found in man, but, as in man, and in the chimpanzee, the vasa recta pass directly from the arcades to the intestinal wall without intercommunicating.[11] Other animals, including the dog, cat and guinea pig, have multiple short vasa recta which abundantly intercommunicate between the arches and the intestinal wall, so that the rabbit has a more favorable morphologic relationship to man than do most other experimental animals.

In the foregoing study we have found that even though abundant replacement of flow through collateral channels may occur after ligation of the rabbit's superior mesenteric artery, the animal always dies with roentgenographic evidence of constantly diminishing flow of blood in the arterial side of the splanchnic circulation. We have postulated that the opening of multiple arteriovenous shunts in the intestinal vasculature of the rabbit following obstruction of its superior mesenteric artery might permit diversion of collaterally-supplied blood away from the bowel wall, with subsequent tissue anoxia and cell death. Shunting is also a satisfactory explanation for the arteriographic demonstration of postligation opacification of the portal vein, and it is further supported by the observation that oxygen saturation of the portal venous blood often rises in the immediate postligation period. The subsequent fall in portal venous blood oxygen saturation and the gradual cessation of arterial flow might be explained on the basis of the development of irreversible shock.

If it is true that interruption of the superior mesenteric artery results in the opening of multiple enteric arteriovenous shunts, then similar hemodynamic changes would be expected in other conditions which also produce severe insult to the mesenteric vascular bed, such as late shock due to any cause, low blood flow states, or marked adrenergic receptor stimulation. We have consulted the investigative literature and have found other evidence for shunting.

Jacobson and his associates,[6] working with rabbits in which they had produced hemorrhagic shock, observed that hyperbaric oxygenation did not significantly increase survival time or alter metabolic manifestations in their animals, suggesting that a primary defect in irreversible hemorrhagic shock is decreased tissue perfusion. Selkurt and co-workers[14,15,16] showed that the dog's splanchnic vascular resistance did not increase during hemorrhagic hypotension. Following retransfusion there was a marked decrease in splanchnic vascular resistance, but values for portal pressure, flow and oxygen content rose, exceeding control figures.

Johnson *et al.*[7] injected glass beads of various sizes into the superior mesenteric arteries of dogs and concluded that closure of enteric arteriovenous anastomoses was of major importance in the reduction of portal flow and pressure by vasopressin. Stimulation of splanchnic nerves in the dog[12] has been shown to produce significant increases in portal pressures and oxygen saturation, suggesting opening of arteriovenous shunts.

Berk and co-workers[3] showed in dogs that the intravenous infusion of epinephrine in amounts sufficient to produce shock, yet capable of being produced endogenously, caused a significant increase in portal vein flow and oxygen pressure. These findings, too, were explained by the opening of multiple arteriovenous shunts. Appel *et al.*,[2] studying various vasoactive drugs including epinephrine and nor-epinephrine, found that these agents increased portal vein pressure, although arteriovenous shunting was not considered as a possible mechanism. The technique of cineportography has been

used in dogs to demonstrate a decreased portal vein clearance time associated with a rise in portal pressure following administration of epinephrine or nor-epinephrine.[8] Child[6] has shown a rise in portal pressure following epinephrine administration in man.

Finally, Boijsen and Redman,[4] studying the effects of epinephrine during celiac and superior mesenteric angiography in man, recently reported that selective injection of epinephrine into the superior mesenteric artery decreased the emptying time of jejunal and ileal branches. Appearance of contrast material in the corresponding veins was improved in about 50 per cent of their studies and these veins disappeared earlier after epinephrine, suggesting a faster flow of opaque material through peripheral branches of the superior mesenteric artery. Although the reasons for this observation are not yet clear, it is again tempting to explain them on the basis of arteriovenous shunting.

In the course of the study reported herein we have been able to identify portal vein opacification after ligation of the superior mesenteric artery. The application of this sign to human diagnosis will require further exploration, for the human portal vein is often opacified on normal mesenteric arteriograms. Perhaps a dose of contrast material can be selected which will not ordinarily visualize the portal vein, but which, under circumstances of mesenteric-portal shunting, might produce a significant and meaningful opacity of the portal venous system. If such a sign can be developed, it might prove especially useful when bowel ischemia exists without definite evidence of organic vascular occlusion.[1]

If arteriovenous shunting is a significant factor contributing to morbidity and mortality in the various conditions of impaired mesenteric blood flow, then need for controlling or lessening the degree of shunting becomes obvious. Several investigators[9,10,13] have demonstrated the efficacy of adrenergic blockade in controlling the metabolic manifestations, and in improving survival rates in such conditions.

Our own future efforts will include an evaluation of adrenergic blocking agents, in the hope that an arteriographic catheter in place in the aorta might be used both for correct diagnosis of abnormal mesenteric flow states and for the administration of a useful therapeutic agent.

SUMMARY

1. Because of anatomic similarities between the splanchnic circulations of man and the rabbit, the rabbit was selected as the subject for experiments involving the nature of splanchnic blood flow after ligation of the superior mesenteric artery.

2. Collateral flow to the obstructed superior mesenteric artery is established almost immediately, as demonstrated by contrast aortography, and circulation usually diminishes until the animal dies. Clotting of blood in mesenteric and collateral channels does not appear to play a role in mortality, for heparinization is not effective in prolonging life.

3. A possible mechanism contributing to bowel ischemia in superior mesenteric artery obstruction is the opening of arteriovenous shunts. Supporting evidence includes opacification of the portal and mesenteric venous systems in experimental animals, which is not observed in control animals who have had repeated arteriography. Additional evidence is offered by portal venous blood oxygen saturation studies performed before and after ligation of the superior mesenteric artery. Since there is a slight rise in portal venous blood oxygenation after ligation, shunting of arterial blood is a not unlikely explanation. Experimental work of other authors pertaining to splanchnic arteriovenous shunting is presented.

4. The possibility of developing portal vein opacification as an arteriographic sign of mesenteric arteriovenous shunting states is discussed. The treatment of shunting states with adrenergic blocking agents

through the arteriographic catheter is considered.

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LYMPHATIC AND VISCERAL IRRADIATION FROM ENDOLYMPHATIC INFUSION IN THE RABBIT*

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NUMEROUS reports of the clinical application of direct endolymphatic therapy[3,4,8,14,25] have appeared since the method was reported by Jantet and associates in 1958.[13,14] Lymph node metastases from melanoma,[3,8] seminoma,[26] carcinoma of the breast,[16] squamous cell carcinoma[16] and primary lymphoma[4,5,25] have been successfully treated with this technique. The rabbit with lymphatic secondary lesions from implanted V×2 carcinoma[15] has proved valuable for studying the oncolytic effect of endolymphatic radiation therapy[7,22] and for comparing the relative effectiveness of isotopes after intralymphatic administration.[22] Destruction of gross lymph node architecture and tumor sterilization has been observed in a high proportion of lymph nodes infused both in man[4] and in the experimental animal.[22,23]

Despite these clear indications of the cancerocidal potential of endolymphatic therapy, complementary studies specifically designed to determine the safety of the technique have hitherto been lacking. In particular, the amount of unintended irradiation of organs other than the target lymph nodes has been only crudely estimated.[8] In man, accurate measurements of the distribution of isotopes administered by the endolymphatic route have been hampered by the inability of externally situated counters to discriminate between the uptakes in deeply seated viscera such as the kidney, spleen, liver and lungs, and the uptake in adjacent retroperitoneal and mediastinal lymph nodes. The extent to which these organs are irradiated is at present unknown.

We have previously described[22] the results of a controlled experiment in which endolymphatic P^{32} (0.8 mc) and I^{131} (4.0 mc) were compared. Both isotopes were highly effective in treating early and moderately advanced lymphatic metastases. The present study was undertaken to determine the lymphatic, visceral and skeletal irradiation after P^{32} and I^{131} infusion into the lymphatics of the rabbit.

METHOD

The distribution of radioactive endolymphatic infusions was studied in 46 rabbits. Twenty rabbits were infused with the I^{131} preparation and 26 infused with the P^{32} preparation.

The infusion technique, which has been fully described elsewhere,[9] delivered a volume of 0.8 to 1.0 ml. into the right saphenous lymph vessel of the rabbit. This volume was sufficient to saturate the single popliteal and the ipsilateral iliac lymph nodes (Fig. 1). Excess contrast medium passed cephalad through the lumbar lymph trunks and thoracic duct to the pulmonary vessels. Contrast material not retained in the lungs entered the systemic circulation.

The I^{131} preparation[9*] consisted of Triolein I^{131} (1 part) dissolved in Ultrafluid Lipiodol† (18 parts). The P^{32} preparation[22*] was a 10 per cent solution of Tri-n-octyl phosphate P^{32} in Ultrafluid Lipiodol. The compound Tri-n-octyl phosphate was selected for infusion because of its anticipated chemical stability *in vivo*.

New Zealand white rabbits (Oryctologus cuniculus) weighing approximately 2 kg. were used in all the experiments. Forty-one of the 46 animals were inoculated in the

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right thigh with the transmissible V×2 carcinoma prior to infusion.[9] The inoculation to infusion interval varied from 9 to 25 days. The primary V×2 carcinoma in the thigh was resected at the time of the infusion.[9] Five normal rabbits were not inoculated with V×2 cell suspension.

The animals were killed between 1 and 65 days after infusion. The popliteal and iliac lymph nodes, lungs, liver, spleen, kidneys and bone samples were then removed and the radioactivity counted. The bone specimens were taken from either the ribs, femur or tibia. Bremsstrahlung and gamma emissions from the postmortem specimens were counted by a sodium iodide scintillation counter. Residual activity in the carcass was measured in a bin mounted with 6 radially arranged Geiger counters. The specific activity of the infusions varied from 0.30 to 1.00 mc per ml. for P^{32} and from 1.00 to 5.00 mc per ml. for I^{131}.

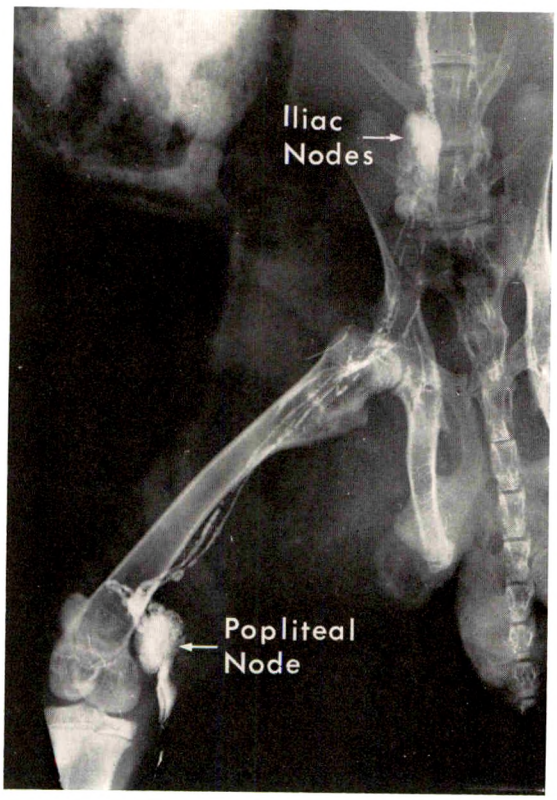


Fig. 1. Infusion into the right saphenous lymph vessel of a rabbit 14 days after V×2 carcinoma implantation into the right thigh. The contrast medium has filled the popliteal lymph node and the iliac lymph nodes. Excess contrast medium has entered the lumbar lymph trunks.

Radioactivity in the blood, urine and feces was determined in 7 rabbits given the P^{32} preparation. Blood samples were obtained from the dorsal marginal ear vein. Fecal and urine specimens were collected continuously in a metabolic cage.

Chemical analysis of the derivatives of Tri-n-octyl phosphate commenced with an assay of the total P^{32} in the plasma or urine specimen by liquid beta counting. The acidified urine or plasma was then extracted with successive aliquots of ether to remove organic P^{32} compounds. The activity not extracted was assumed to be inorganic phosphate. The activity associated with the ether extracts was chromatographed on a silica gel column to separate Tri-n-octyl phosphate from Mono-octyl phosphate and Di-octyl phosphate.

RESULTS

LYMPH NODES

The mean uptake in either the popliteal or the iliac lymph nodes was approximately 10 per cent of the administered dose per gram of lymph node, irrespective of the isotope infused (Table 1). Lymphograms taken immediately after infusion (Fig. 1) showed contrast medium beyond the iliac lymph nodes in each case, indicating that the capacity of the lymph nodes to retain the contrast material had been exceeded. Under the conditions of these experiments (*i.e.*, V×2 involved lymph nodes), 0.1 ml. of infusion was therefore sufficient to saturate 1 gram of lymph node tissue.

The energy of lymph node beta irradiation was calculated from these uptake values by the formula:[10]

$$\text{Beta-particle dose (rads)} = K\text{-beta} \times C_o \times (T_{eff}/T_p),$$

where K-beta is a constant for each isotope, K-beta for $P^{32} = 730$; K-beta for $I^{131} = 110$.

C_o is the initial concentration of the isotope in microcuries per gram.

TABLE I

UPTAKE OF P^{32} AND I^{131} IN THE POPLITEAL AND ILIAC LYMPH NODES

Specimen	P^{32}				I^{131}			
	No. of Specimens	Per cent Administered Dose	Per cent Administered Dose / gm.	Energy* Equivalent	No. of Specimens	Per cent Administered Dose	Per cent Administered Dose / gm.	Energy* Equivalent
Popliteal Lymph Node								
Mean		2.68	10.12	73,000		4.96	7.90	44,000
Standard deviation	22	9.65	9.70	72,000	18	7.20	6.72	37,000
Minimum		0.17	1.70	13,000		0.20	0.03	165
Maximum		16.60	42.10	320,000		30.00	35.70	195,000
Iliac Lymph Nodes								
Mean		5.41	10.22	73,000		7.45	10.50	58,000
Standard deviation	19	3.70	7.60	58,000	16	7.36	8.63	47,000
Minimum		0.32	0.16	1,200		1.20	0.34	1,850
Maximum		12.50	26.50	190,000		25.50	24.10	130,000

* Energy equivalent calculated on the basis of a 1.0 mc infusion of P^{32} and 5.0 mc of I^{131}.

T_{eff} is the effective half life and T_p is the physical half life.

This formula gives a good approximation to total lymph node irradiation ignoring the unimportant gamma and Bremsstrahlung contribution.[9]

The energies equivalent to the uptakes are also shown in Table I. The maximal irradiation received by a single lymph node was 320,000 rads. Several other lymph nodes received in excess of 200,000 rads. The over-all mean lymph node irradiation was approximately 73,000 rads after 1 mc of P^{32} and 55,000 rads after 5 mc of I^{131}.

Since the energy absorbed by the lymph nodes varied directly as the specific activity of the infusate, energies even greater than those shown in Table I could easily be achieved. The limited penetration of beta particles in tissue virtually confined the radiation energy to the infused lymph nodes. Radiation doses vastly in excess of those necessary for oncolysis were thus delivered to the lymph nodes with safety. Radiation doses of this order caused actual cell and lymph node destruction[22,23] rather than the limited proliferative ability[27] characteristic of less energetic radiotherapeutic techniques.

LUNGS

The proportions of the administered doses which reached the lungs were 6.1 ± 7.9 per cent of the P^{32} administered and 5.2 ± 6.2 per cent of the I^{131}. These dosages were equivalent to 0.33 ± 0.44 per cent (P^{32}) and 0.35 ± 0.48 per cent (I^{131}) per gram of lung (Table II). The equivalent energies were $2,300 \pm 3,100$ rads (P^{32}) and $2,000 \pm 2,700$ rads (I^{131}).

Although occasionally encountered in conventional radiotherapeutic practice, *e.g.*, in the treatment of mammary cancer, serious pulmonary radiation is a potential hazard with endolymphatic therapy. However, the proportion of the infusion which reaches the lungs in man is not as high as that found in these rabbits.[16] The human

TABLE II

VISCERAL AND SKELETAL UPTAKES OF P^{32} AND I^{131} AFTER ENDOLYMPHATIC INFUSION

	P^{32}			I^{131}		
	No. of Specimens	Per cent Administered Dose/gm.	Energy* Equivalent (rads)	No. of Specimens	Per cent Administered Dose/gm.	Energy* Equivalent (rads)
Lungs						
Mean		0.33	2,300		0.35	2,000
Standard deviation	24	0.44	3,100	20	0.48	2,700
Minimum		0.002	15		0.01	55
Maximum		1.81	13,700		1.41	8,000
Kidneys						
Mean		0.015	115		0.004	20
Standard deviation	21	0.030	220	14	0.003	15
Minimum		0.0001	1		0.0002	1
Maximum		0.130	920		0.012	70
Skeleton						
Mean		0.001	7		0.0024	12
Standard deviation	24	0.014	100	8	0.001	5
Minimum		0.0002	1		0.002	10
Maximum		0.040	300		0.005	30
Liver						
Mean		0.008	60		0.005	30
Standard deviation	26	0.020	150	17	0.014	65
Minimum		0.0001	1		0.0001	0.5
Maximum		0.08	600		0.06	330
Spleen						
Mean		0.019	150		0.015	60
Standard deviation	23	0.014	100	8	0.042	200
Minimum		0.002	15		0.0002	1
Maximum		0.040	300		0.120	660

* Energy equivalents calculated on the basis of a 1.0 mc infusion of P^{32} and 5.0 mc of I^{131}.

infusion technique is monitored by either a collimator counter or by fluoroscopy and the infusion stopped when the contrast medium is observed to enter the major lymph ducts. Furthermore, the volume of infusion reaching the lungs is a function of the initial volume infused into the lymphatics.[12] The rabbits in these experiments were thus at a considerable disadvantage, receiving 0.5 mc/kg. compared with less than 0.1 mc/kg. in man. In man, the proportion of the administered dose reaching the lungs is usually less than 6 per cent, most of which is cleared within the first week.[16]

SYSTEMIC CIRCULATION

Radioactivity was estimated in samples of venous blood taken from 7 animals infused with the P^{32} preparation. Immediately after endolymphatic infusion, the

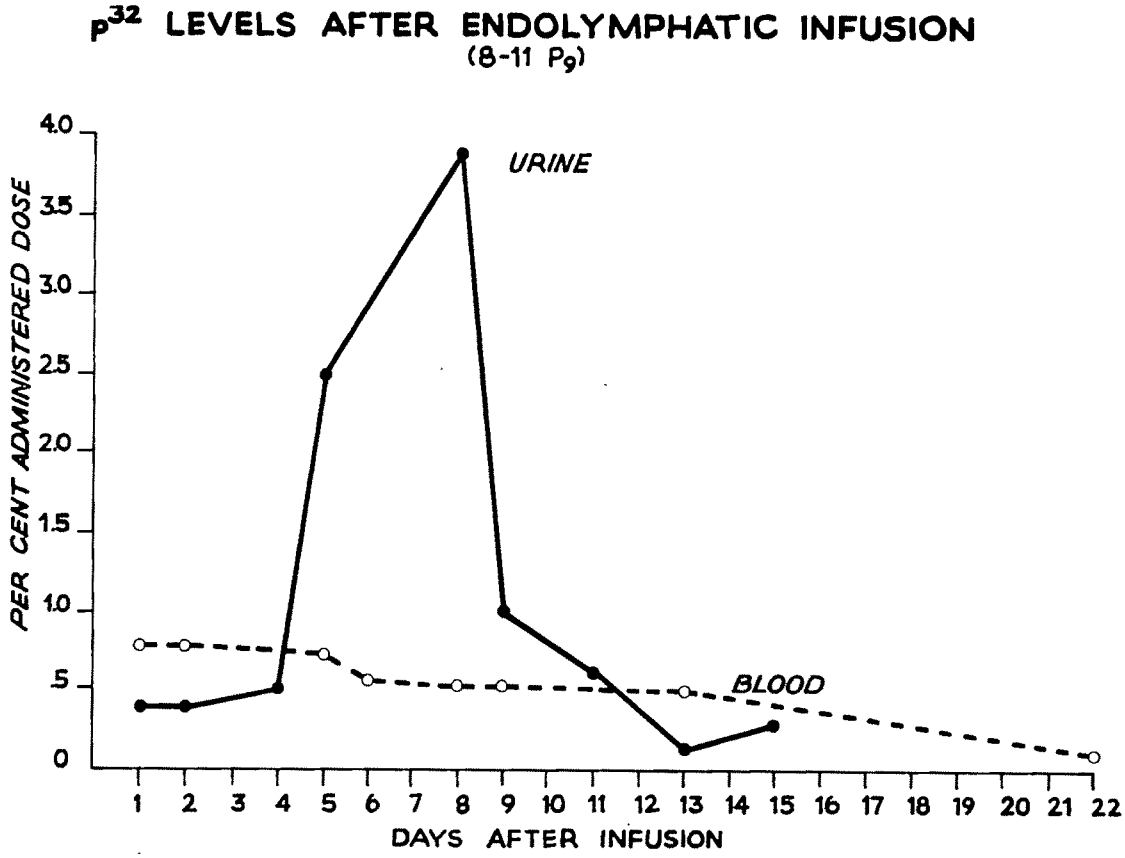


FIG. 2. Concentrations of P^{32} in the blood (per cent administered dose per hundred ml.) and urine (per cent administered dose excreted per day) of a rabbit after endolymphatic infusion. The total quantity of P^{32} in the circulation is also represented by the broken line since the blood volume was approximately 100 ml.

samples were taken daily thereafter as appropriate. Sampling was discontinued when the radioactivity was unrecordable in a 5.0 ml. blood sample or on the prior death of the rabbit. The quantity of isotope in the systemic circulation was reasonably constant initially and then gradually fell over several weeks (Fig. 2). The highest concentration achieved was 2 per cent of the administered dose. Comparable trends and concentrations were found in other experiments[5,9,21] after infusion of I^{131}. Measurements of urinary radioactivity (Fig. 2) showed that the mean daily urinary clearance of P^{32} was at least as great as the total amount of P^{32} in the circulating blood. Mean daily clearance of isotope from the circulation was therefore quantitatively of the same order as the mean amount of isotope in the general circulation at any time.

The additional P^{32} entering the systemic venous blood must have passed through the pulmonary vascular bed from lymphoid tissue and other viscera, including the lungs themselves. The mean daily excretion was about 1.5 per cent of the administered dose. Since the blood concentration was reasonably stable, the mean daily excretion was therefore equivalent to the minimum mean daily total body mobilization of P^{32}.

EXCRETION

The kidneys were the major route of elimination of the P^{32} compounds. Fecal P^{32} amounted to less than 5 per cent of that in the urine so that elimination in the feces

was of comparatively minor importance. Fecal radioactivity may have represented excretion by the liver.

The rate of urinary excretion varied, the daily mean of the 7 animals being 1.5 per cent of the administered dose. Peak excretion occurred between 1 and 7 days after infusion (Fig. 2). Other investigators[20,26] similarly observed peak excretion of I^{131} in the first week after intralymphatic infusion.

The daily excretion rate of 1 to 2 per cent indicated that half of the administered dose was eliminated within 25 to 30 days of infusion; *i.e.*, the total body biologic half life of the preparation was 25 to 30 days. Physical decay alone reduces 1.0 mc of P^{32} to 125 μc after 40 days. The combined effect of physical decay and renal excretion was to reduce a 1.0 mc P^{32} infusion to a safe 60 μc of whole body radioactivity 6 weeks after infusion.

KIDNEYS

Uptakes of P^{32} and I^{131} by the kidneys were low (Table II). The absorbed energies equivalent to these uptakes are not nephrotoxic according to the criteria of other authors.[11,17] Alternative calculations of the renal radiation derived from the quantities of radioactive urine excreted indicated that less than 300 rads were delivered to the kidneys.

SKELETON

Samples of bone were taken from 32 rabbits and the uptakes counted (Table II). Skeletal radiation was low with either isotope. Because free orthophosphate tends to localize in bone,[19] the stability of Tri-n-octyl phosphate *in vivo* was determined both in the rabbit and in man (Table III). Some degradation to orthophosphate and mono- and di-octyl phosphate occurred in all cases. The proportion of free orthophosphate was greater in man than in the rabbit, so that marginally, greater irradiation may be received by the human skeleton.

Since the introduction of P^{32} orthophosphate for the treatment of polycythemia vera by Lawrence in 1940[18] a wide experience has been gained with the intravenous use of this isotope. Recently several authors have drawn attention to the risks of marrow failure and myeloproliferative dis-

TABLE III

THE RELATIONSHIP BETWEEN TRI-N-OCTYL PHOSPHATE AND ITS DERIVATIVES AFTER ENDOLYMPHATIC INFUSION IN THE RABBIT AND IN MAN

	Days After Infusion	Orthophosphate (per cent)*	Mono-octyl and Di-octyl Phosphates (per cent)*	Tri-n-octyl Phosphate (per cent)*
Rabbit No. 1				
Plasma	12	2.9	61.1	36.0
Urine	12	59.8	30.2	10.0
Rabbit No. 2				
Plasma	12	4.5	78.5	17.0
Urine	12	65.4	18.0	16.6
Mrs. A				
Plasma	1	44.0	38.6	17.4
Urine	1	48.0	52.0	Nil
Plasma	4	50.0	35.9	14.1
Urine	4	40.0	53.9	6.1

* Percentage of total quantity in plasma or urine.

orders occurring several years after P^{32} treatment.[19,28] However, the intravenous injection of large quantities (c. 15 mc) of radioactive orthophosphate into patients with an unstable bone marrow is clearly not comparable to endolymphatic infusion with small doses of Tri-n-octyl phosphate. The mean uptake of I^{131} in the rabbit's skeleton was not less than that of P^{32}, suggesting that any special avidity of the skeleton for the P^{32} compounds (in particular orthophosphate) was compensated for by the lymphoid and pulmonary filters encountered after endolymphatic infusion. The skeleton is responsible for some 8.6 per cent of the weight of a rabbit.[6] Only a small proportion of either isotope, therefore, localized in the skeleton.

LIVER AND SPLEEN

The liver and spleen both recorded low uptakes of isotopes (Table II). The energies equivalent to these uptakes are insufficient to cause significant or permanent lesions to either viscus.[1,23,24]

RESIDUAL CARCASS

The radioactivity in the carcass was measured after the removal of the popliteal and iliac lymph nodes, lungs, liver, spleen, kidneys and the small bone samples. In the P^{32} group, 15.2 ± 17.8 per cent of the administered dose remained in the carcass. The corresponding values for the I^{131} group were 24.6 ± 16.5 per cent of the administered dose. The radiation energies equivalent to these values are low (Table II).

CONCLUSIONS AND SUMMARY

Dosimetric studies have been carried out in 46 rabbits after endolymphatic infusions of P^{32} and I^{131} in Ultrafluid Lipiodol. There were no important differences between the behaviour of the isotopes.

Greatest uptakes were recorded by the popliteal and iliac lymph nodes (mean of approximately 10 per cent of the administered dose per gram of lymph node). The energies equivalent to the mean lymph node uptakes (73,000 and 55,000 rads) greatly exceeded the radiation doses possible with other forms of radiotherapy. In some lymph nodes the absorbed irradiation reached hundreds of thousands of rads.

The irradiation received by most other viscera and the carcass generally was trivial by comparison. The lungs recorded uptakes at levels which were high because of the large volumes injected.

The major route of the P^{32} compounds was by the kidneys. Daily excretion rates varied considerably but were usually about 1 to 2 per cent of the administered dose per day. Calculations based on either renal uptakes or renal excretion rates indicated that the quantities of irradiation received ought not to be nephrotoxic.

The concentration of P^{32} in the blood declined from a peak of 1 to 2 per cent of the administered dose per 100 ml. in the first week to unrecordable levels over the succeeding 3 to 5 weeks. Tri-n-octyl phosphate was found to be unstable in plasma and in urine. Despite this instability, no significant localization of P^{32} in the skeleton was apparent.

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SERIAL BRAIN SCANNING WITH TECHNETIUM 99m AND SCINTILLATION CAMERA*

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IT IS evident that the use of a scintillation camera and a short-lived radionuclide such as technetium 99m (Tc^{99m}) has many advantages over the conventional scanner, particularly in brain scanning. It permits the examination of severely ill, agitated and uncooperative or young patients. Multiple views are easily obtained, and, in addition, a rapid imaging has made possible serial scintiphotography. Utilizing this approach, dynamics of an isotope bolus as it traverses the normal and pathologic vasculatures can be sequentially visualized.[6,8] Furthermore, the read-out mode provided by the 1,600 channel analyzer permits digital assessment of the time course of isotope uptake in multiple sites in the scintiphotograph. Such a dynamic approach is expected to substantially increase the diagnostic accuracy in brain scanning.

In the present paper the results of serial brain scanning and analysis of the uptake pattern by the use of a scintillation camera and Tc^{99m} are summarized. In some cases, xenon 133 (Xe^{133}) and I^{131}-labeled macroaggregates of human serum albumin (MAA-I^{131}) were also used for brain scanning in an attempt to determine the vascular characteristics of brain lesions.

MATERIAL AND METHOD

The studies were performed on patients under the care of the Department of Neurosurgery, exclusively at the Central Radioisotope Division of Kyoto University Hospital.

Tc^{99m} SCANNING

Tc^{99m} pertechnetate* in doses of 5 to 10 mc was injected into the antecubital vein as a bolus. The scintillation camera† was set to image either the anteroposterior or lateral view. The head was fixed to the table with an adhesive tape. Serial scintiphotographs were obtained immediately after, 2 or 3, 5, 10, 15, 30, 45, 60 and, occasionally, 90 and 120 minutes after the injection, accumulating 10×10^4 or 15×10^4 counts for each exposure. At the same interval, accumulation for 60 seconds each and immediate read-out on the paper tape were performed with the memory scope and the 1,600 channel multiparameter analyzer. In addition, rapid serial 3 or 4 second exposures were obtained using a 35 mm. film.

Determination of uptake ratio. From among the serial scintiphotographs, the one in which the focus was best demarcated was selected and the corresponding paper tape record of count rates was rearranged on the sheet with a matrix of 40 by 40. Referring to the scintiphotograph and the count rate sheet,[4] the uptake ratio was calculated as follows:

$$\text{Uptake ratio} = \frac{F}{B}\ (\text{arbitrary unit}),$$

where F = total counts in the matrix of 3 by 3 which showed the highest count rates in the focus and, B = total counts in the matrix of 3 by 3 which showed the lowest count rates in the apparently normal brain.

Uptake ratios were calculated for the rest of the serial scintiphotographs using the same co-ordinates for the 2 sets of 3 by 3 matrices, one for the focus and the other for the normal brain.

MAA-I^{131} SCANNING

MAA-I^{131}‡ in doses between 50 and 100

* Dainabbott RI Laboratories, Tokyo.

† Pho/Gamma III, Nuclear Chicago Co., Des Plaines, Ill.

‡ Macroscan-131. Dainabbott RI Laboratories, Tokyo.

* From the Department of Neurosurgery and the Central Radioisotope Division, Kyoto University Medical School and Hospital, Kyoto, Japan.

μc diluted with physiologic saline to 5 to 10 cc. was injected into the carotid artery employing a 19 gauge needle. The anteroposterior and lateral scintiphotographs of the head and the anteroposterior scintiphotograph of the chest were obtained immediately after the injection. Map and profile pictures and 1,600 channel count rate read-out data also were obtained. In several cases, MAA-I^{131} scanning was performed by the use of a conventional rectilinear scanner.§

When injected into the vessels, macroaggregates of human serum albumin are filtered out by the capillaries of the target organ. If the aggregates labeled with I^{131} are injected into the internal carotid artery, their accumulation in the brain can be externally collimated, and their distribution is expectedly proportional to the volume of perfused capillary bed of the brain.[3,7]

Thus, it seems evident that the hot focus in a MAA-I^{131} scintiphotograph indicates a high vascularity in the lesion. When a considerable size of arteriovenous shortcircuit exists in the focus, a corresponding amount of MAA-I^{131} is shunted away through the fistula, and the focus may not be hot, but may appear cold. In this event, however, a shunted part of MAA-I^{131} is eventually entrapped in the pulmonary vascular bed and can be detected easily by scanning the chest.

In the present study, the following assumptions are made: when the brain and pulmonary scannings are performed following the intracarotid injection of MAA-I^{131}, a hot focus in the brain represents a densely vascularized lesion, and a cold brain focus, without significant radioactivity in the lung, suggests a lesion with poor vascularity. High radioactivity in the lung, irrespective of whether the brain focus is hot or cold, indicates the existence of arteriovenous shunts in the territory of supply of the injected artery, or most probably in the pathologic lesion.

§ Scintillation Scanner Type SCC-30. Shimadzu Co., Kyoto.

Xe^{133} scanning

Xe^{133}‖ in doses of 5 to 10 mc dissolved in 10 cc. of saline was injected into the carotid artery over a 30 second period. The scintillation camera was set to image the anteroposterior or lateral view during the injection period. The count rates accumulated during this period were printed out in the following 45 seconds. A second scintiphotograph and accumulation were obtained for the next 30 seconds (75–105 seconds after the onset of injection) and a print-out was made during the following 45 seconds. The procedures were repeated, covering a period of 15 to 20 minutes.

A 35 mm. film was exposed at the speed of 1 frame for each 30 second period. The whole series covered a period of 12 to 18 minutes starting from the onset of injection.[9]

RESULTS

Serial Tc^{99m} scanning

The chronologic patterns of the serial scintiphotographs are classified into 3 types. Type I lesion is characterized by the maximum uptake in the earliest phase followed by a gradual decrease. Meningiomas, arteriovenous anomalies and hemangiomas belong to this type. In Type II lesion the focus becomes progressively more dense. This is observed in gliomas, sarcomas, cerebral infarctions, brain abscesses and most of the metastatic carcinomas. Type III lesion consists of a persistently cold focus and is experienced in intracerebral hematoma and cystic lesions.

Figure 1, *A–D* represents a series of lateral scintiphotographs in a case of arteriovenous malformation. The arteriovenous anomaly in the right sylvian region and drainage vessels, mainly the posterior portion of the superior sagittal sinus and the torcular Herophili, were well shown by increased radioactivity in the 1 minute scintiphotograph (Fig. 1*A*). A few minutes later, a scintiphotograph (Fig. 1*B*) became equivocal, showing a moderate concentra-

‖ Xeneisol-133. Union Carbide Co., Tuxedo, N. Y.

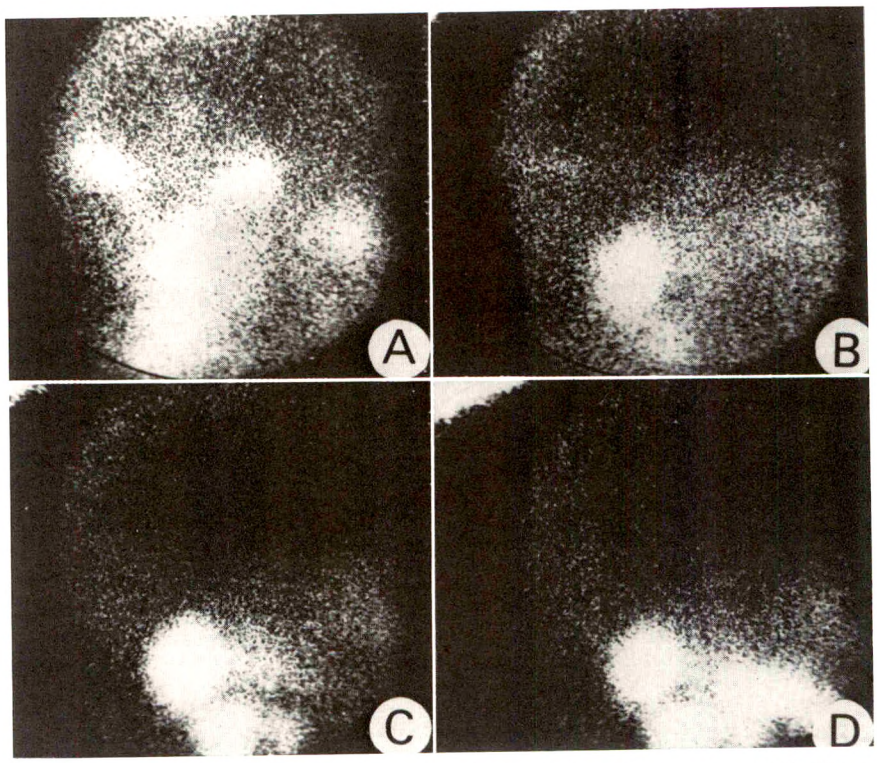


FIG. 1. Tc^{99m} serial scans of arteriovenous malformation in the right sylvian region. Right lateral view. Note that the highest radioactivity in the malformation and drainage vessels is seen in the 0–1 minute scintiphotograph (*A*). (*B*) 5–6, (*C*) 60–61, and (*D*) 120–121 minutes after the intravenous injection of 10 mc of Tc^{99m}.

tion of tracer in the torcular Herophili region. Later scintiphotographs (Fig. 1, *C* and *D*) were essentially normal.

Figure 2 illustrates 3 second serial exposure records in the same patient. The arteriovenous malformation and drainage vessels were best shown during the initial cerebral circulation of Tc^{99m} injected as a bolus.

Arteriovenous malformations are best demonstrated in the earliest scintiphotographs taken following a rapid intravenous injection of Tc^{99m}. Although the angiographic studies which provide precise morphologic information, such as the type, size and location of the lesion or the anatomy of the main feeding and draining vessels, are indispensable for the diagnosis of cerebral arteriovenous malformations, all of the 7 cases in the present series showed a definite abnormality in the scintiphotographs taken immediately after administration of Tc^{99m}. Thereafter, the abnormal concentration of radioactivity showed an acute decrease, and later scintiphotographs tended to normalize rapidly.

In meningiomas and cavernous angioma, the chronologic pattern of serial scintiphotographs is essentially similar to that of arteriovenous malformation. The meningioma appears immediately or shortly after the intravenous injection of Tc^{99m} as a localized, dense and homogeneous focus with a clear margin. After this, the focus loses its high radioactivity more or less rapidly, but the lesion generally remains distinct at the end of the serial studies covering 60 to 120 minutes after the injection (Fig. 3, *A–F*). In some cases, however, the fall in radioactivity is so rapid that the lesion practically disappears in 60 to 120 minutes, as illustrated in Figure 4, *A–D*.

Angiographic and histologic studies show that no exact parallelism exists between the intensity of radioactivity in the focus and

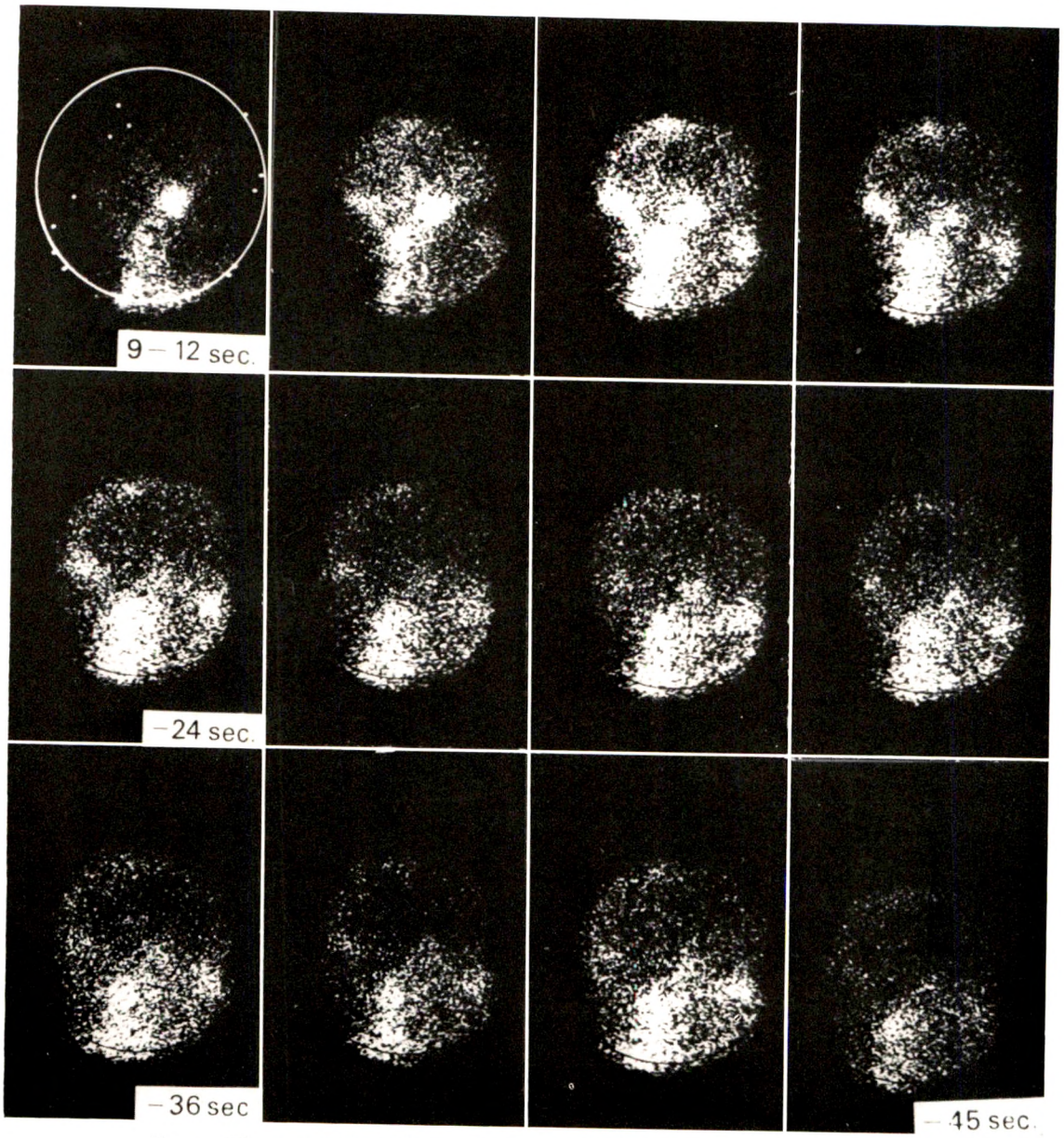


Fig. 2. Three second serial exposure records in the same case as in Figure 1. Right lateral view.

the vascularity of tumor.

Astrocytomas and oligodendrogliomas show the pattern of progressive accumulation of radioactivity. Figure 5, *A–F* illustrates a series of scintiphotographs in a case of astrocytoma. Initially, the scintiphotographs were equivocal (Fig. 5, *A* and *B*); 15 minutes later, however, a blurred uptake was noted in the central region (Fig. 5*C*). Following this, the uptake gradually increased and the scintiphotographs after 30 minutes showed a clear active focus (Fig. 5, *D–F*).

A similar pattern is noted also in cerebral infarction, as illustrated in Figure 6, *A–F*. A carotid angiogram showed an avascular focus in the right occipital region. The scintiphotograph obtained 1 minute after injection (Fig. 6*A*) showed that the cold central focus in the occipital region was

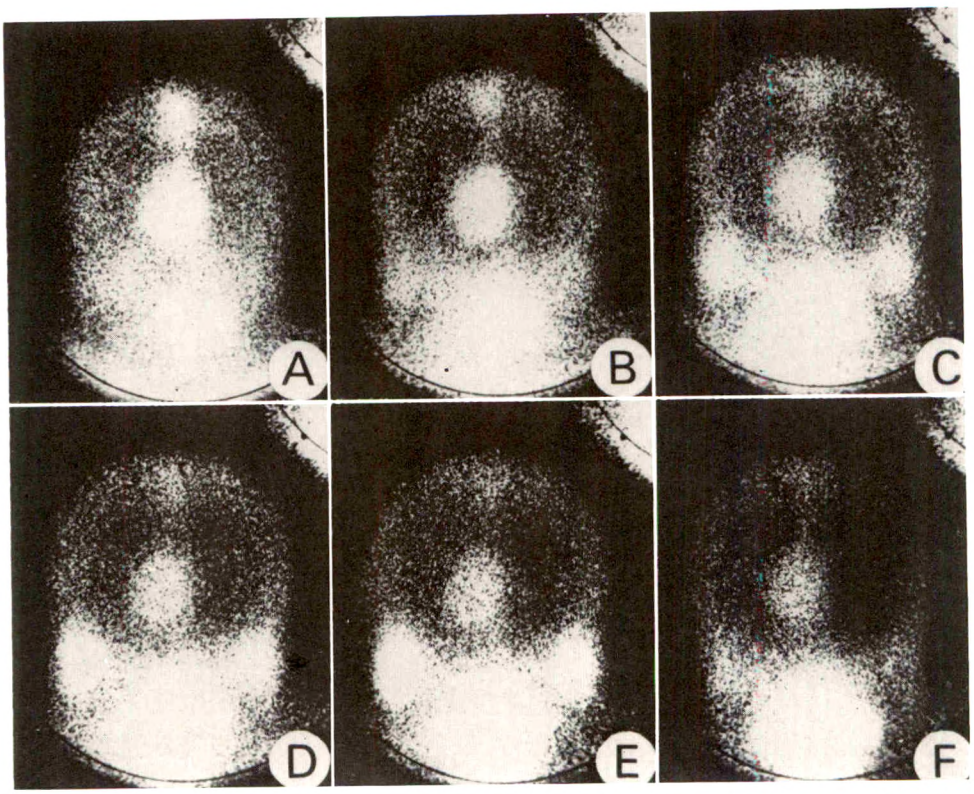


FIG. 3. Tc^{99m} serial scans of frontal parasagittal meningioma. Anteroposterior view. Note the sharply demarcated, dense, homogeneous focus characteristic of meningioma. (*A*) 0–1, (*B*) 5–6, (*C*) 15–16, (*D*) 30–31, (*E*) 60–61, and (*F*) 90–91 minutes after the intravenous injection of 10 mc of Tc^{99m}.

surrounded by a zone of increased radioactivity which apparently corresponded to the perifocal hyperemic area observed on the angiogram. With time, the central focus of softening slowly became impregnated (Fig. 6, *B–E*), and reached the maximum intensity at the end of the serial studies, 120 minutes after the intravenous administration of Tc^{99m} (Fig. 6*F*).

Glioblastomas and sarcomas usually produce early and active foci, but the radioactivity, unlike that of meningiomas, seems to increase with time (Fig. 7, *A–E*). In carcinomas the results are less uniform. A pattern of progressive increase in uptake was seen in most of the cases (Fig. 8, *A–F*). In a few cases, however, the uptake decreased with time (Fig. 9, *A–F*).

In gliomas, the foci are sometimes dense and uniform but more frequently they are ill-defined and have irregular margins. Gliomas in general showed a pattern of progressive accumulation of radioactivity, in serial scintiphotographs. An exception was the case of oligodendroglioma in which the serial scintiphotographs showed a rather regressive accumulation in the focus (Fig. 10, *A–F*; 11′ in Fig. 12; and Fig. 13*C*). Carotid angiography in this particular case demonstrated a highly vascular midline tumor with arteriovenous shunts.

In Type III lesions the focus remains cold throughout the course of the serial studies. Figure 11, *A*, *B* and *C* demonstrates Tc^{99m}, MAA-I^{131} and Xe^{133} scintiphotographs in a case of frontal intracerebral hematoma due to ruptured angiomatous malformation. The focus was persistently cold in the serial Tc^{99m} studies.

FOCUS-TO-BRAIN UPTAKE RATIO

The uptake ratio patterns are classified into 4 main groups. Characteristic samples are illustrated in Figure 12.

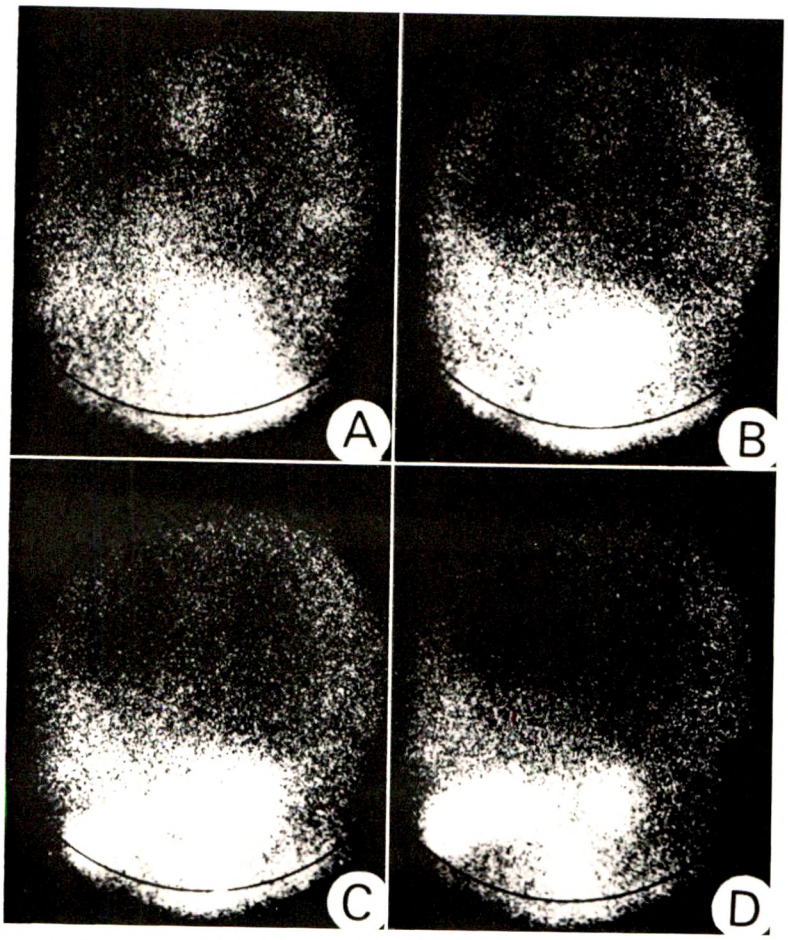


Fig. 4. Tc^{99m} serial scans of parasagittal meningioma. Left lateral view. Note the rapid fall of radioactivity in the successive studies. (*A*) 0–1, (*B*) 20–21, (*C*) 60–61, and (*D*) 120–121 minutes after the intravenous injection of 10 mc of Tc^{99m}.

In Group I, the uptake ratio showed the highest value immediately or shortly after administration of Tc^{99m}, then it decreased more or less rapidly. This group corresponds to Type I focus in the visual classification of serial scintiphotographs, and includes the arteriovenous malformations, meningiomas and cavernous angioma.

In all 7 cases of arteriovenous anomalies, the uptake ratio showed the maximum value immediately after the intravenous injection of Tc^{99m} (0–1 minute read-out), decreased rapidly, and reached the plateau in 5 to 15 minutes. The uptake ratio thereafter remained essentially unchanged (1-a in Fig. 12; and Fig. 13*A*). The maximum value of uptake changed widely, ranging between 1.5 and 6.0.

In 8 out of 10 cases of meningiomas and cavernous angioma, the uptake ratio showed an initial increase, reached the maximum in 5 minutes (6 cases) to 10–15 minutes (2 cases), then decreased (1-b in Fig. 12). In 1 case of meningioma, the uptake ratio was maximum immediately after injection. The remaining case of meningioma was unusual in that the uptake ratio showed a gradual increase throughout the course of serial studies up to 60 minutes (Fig. 13*B*).

As far as the uptake patterns are concerned, Type II foci with progressive accumulation of radioactivity are subdivided into 2 groups (Groups II and III).

In Group II, the uptake ratio tended to increase linearly during the course of serial

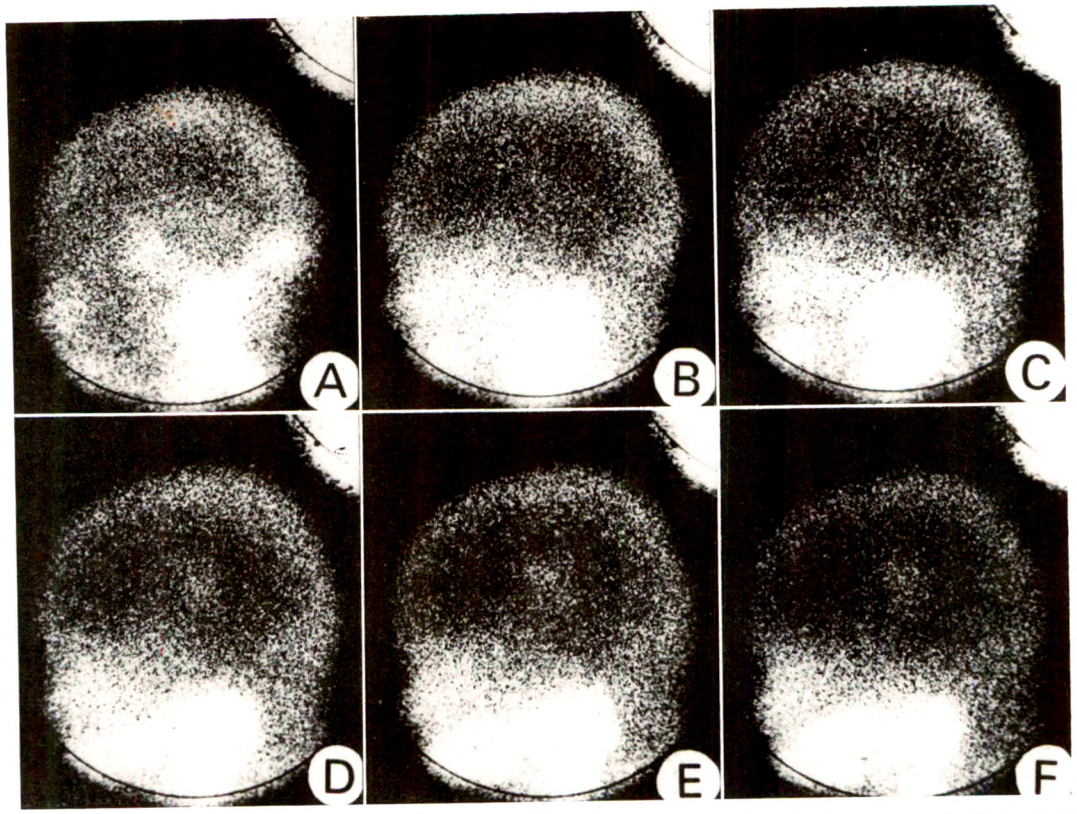


FIG. 5. Tc^{99m} serial scans of astrocytoma. Left lateral view. Note the progressive accumulation of radioactivity. (*A*) 0–1, (*B*) 5–6, (*C*) 15–16, (*D*) 30–31, (*E*) 60–61, and (*F*) 120–121 minutes after the intravenous injection of 10 mc of Tc^{99m}.

studies or reached the plateau in 30 to 60 minutes (II in Fig. 12; and Fig. 13*C*). This type of uptake was observed in benign gliomas and cerebral infarction, except for the 1 case of oligodendroglioma illustrated in Figure 10, *A-F*. In this particular case, the uptake followed a regressive course much the same as in an arteriovenous malformation (II′ in Fig. 12).

Group III comprises the glioblastomas, metastatic carcinomas and sarcomas. The uptake ratio showed an initial increase similar to that in Group II foci, but this was followed by a decrease. The maximum value of uptake was reached usually in 30 to 45 minutes after an intravenous dose of Tc^{99m} (III in Fig. 12; and Fig. 13*D*). In 1 exceptional case of ethmoid cell carcinoma extending intracranially, the uptake ratio showed a regressive course similar to a meningioma (Fig. 9, *A-F*; and III′ in Fig. 12). It is interesting to note that the preoperative diagnosis in this case was an olfactory groove meningioma extending into the ethmoid cells. The tumor showed an abundant blood supply from the hypertrophied ophthalmic artery and the homogeneous tumor stain remained in the venous phase of the angiography, although the demonstration of arteriovenous fistulas might have been atypical of meningioma.

Group IV focus corresponds to Type III lesion in serial scintiphotographs. Spontaneous intracerebral hematoma is an example of this group of uptake pattern (Fig. II, *A*, *B* and *C;* and IV in Fig. 12). The focus continued to be cold during the course of study and the uptake ratio remained below 1.0 with negligible fluctuation. Type III foci were observed also in brain abscesses and cystic tumors. Unfortunately, serial read-out data were not

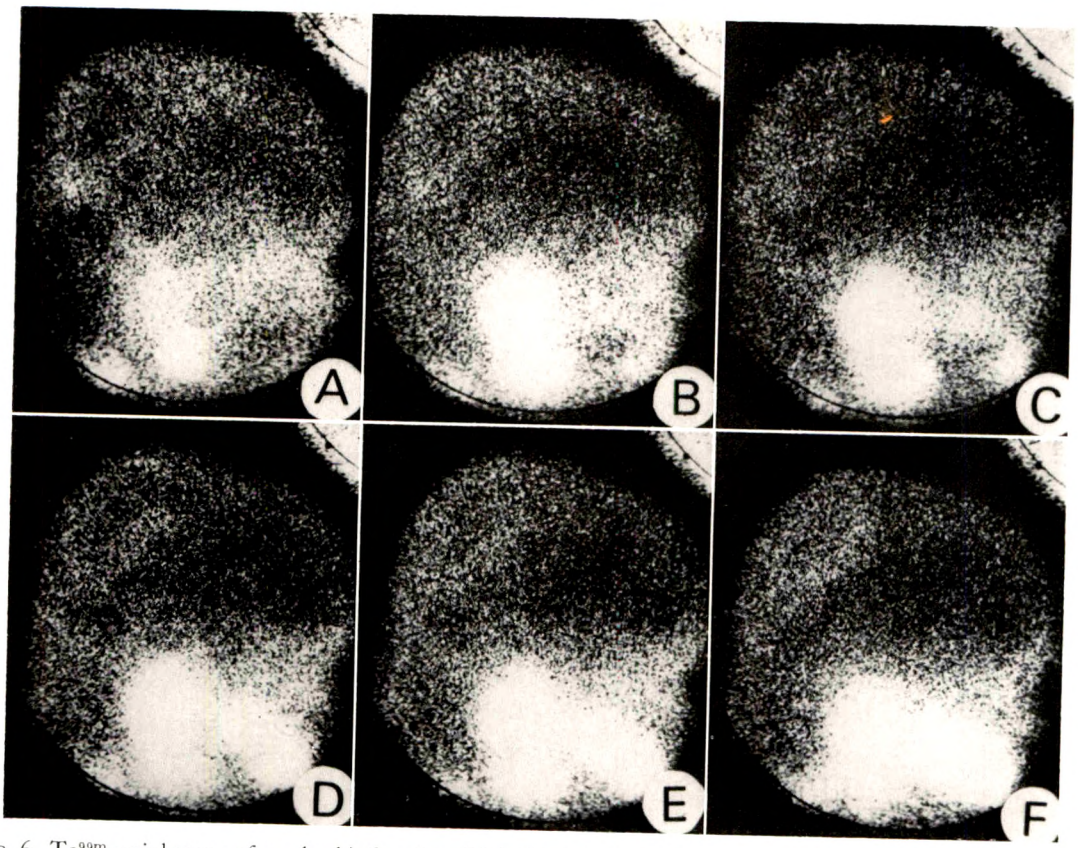


Fig. 6. Tc^{99m} serial scans of cerebral infarction. Right lateral view. Note the cold focus in the occipital region surrounded by a zone of high radioactivity in *A* (0–1 minute scintiphotograph). Progressive accumulation of radioactivity was observed in later studies. (*B*) 15–16, (*C*) 30–31, (*D*) 45–46, (*E*) 60–61, and (*F*) 120–121 minutes after the intravenous injection of 10 mc of Tc^{99m}.

available in these cases, but it seems apparent that the uptake ratio, if it were determined, should have remained less than the unit.

MAA-I^{131} and Xe^{133} scanning

In arteriovenous anomalies, the focus was cold in MAA-I^{131} scans. The pulmonary scan always demonstrated the passage of a large amount of MAA-I^{131} to the lungs. In Xe^{133} scanning, the focus was hot during the 30 second period of intracarotid injection, but the clearance was so rapid in the focus that it became cold in the second scintiphotograph.

In meningiomas, MAA-I^{131} brain scanning showed a hot focus when the feeding artery was punctured. In some cases positive lung scans were obtained also, suggesting the existence of arteriovenous short-circuits in the tumor (Fig. 14, *A*, *B* and *C*). Since meningiomas are generally supplied mostly by the external carotid branches, the tumor, which showed a typical regressive pattern in Tc^{99m} serial studies, may appear cold in either MAA-I^{131} or Xe^{133} scans, if the injection is made not into the external but into the internal carotid artery.

In most of the cases with Group II and IV lesions, the focus was poorly vascularized as judged by MAA-I^{131} and Xe^{133} brain scans. A composite picture of Figure 11 illustrates a case of spontaneous intracerebral hematoma. As described previously the focus remained cold, and the uptake ratio was approximately 0.8 during the course of serial Tc^{99m} studies. In Xe^{133} scanning, the focus was definitely cold during the 30 second period of intracarotid in-

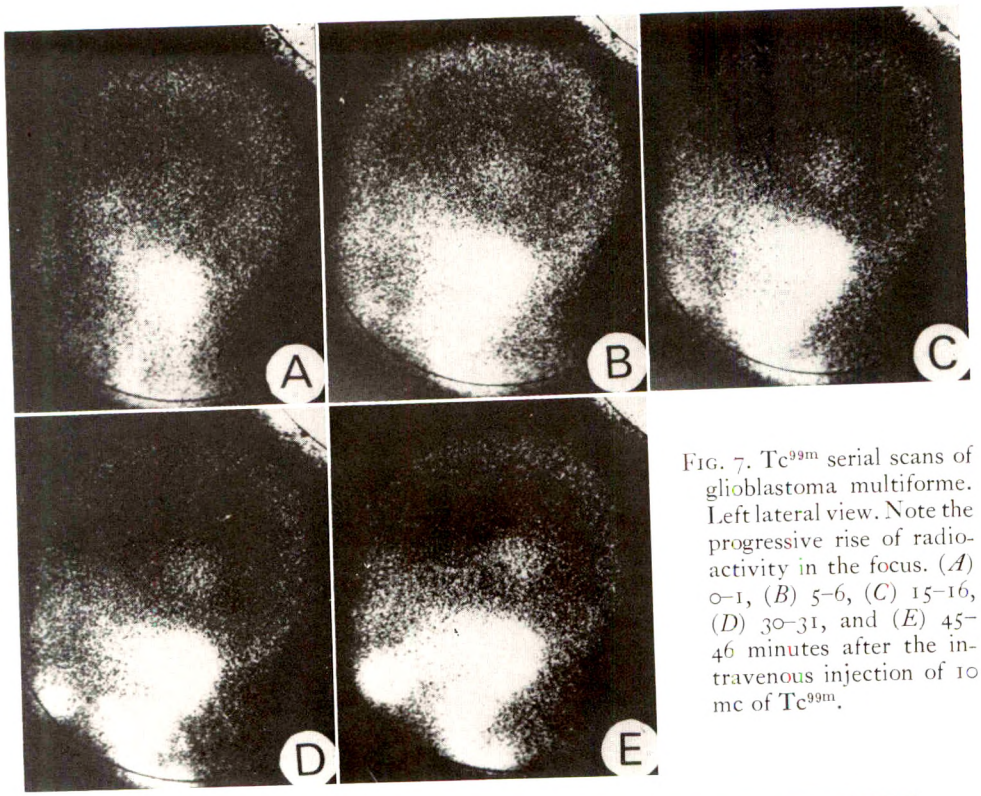


FIG. 7. Tc^{99m} serial scans of glioblastoma multiforme. Left lateral view. Note the progressive rise of radioactivity in the focus. (*A*) 0–1, (*B*) 5–6, (*C*) 15–16, (*D*) 30–31, and (*E*) 45–46 minutes after the intravenous injection of 10 mc of Tc^{99m}.

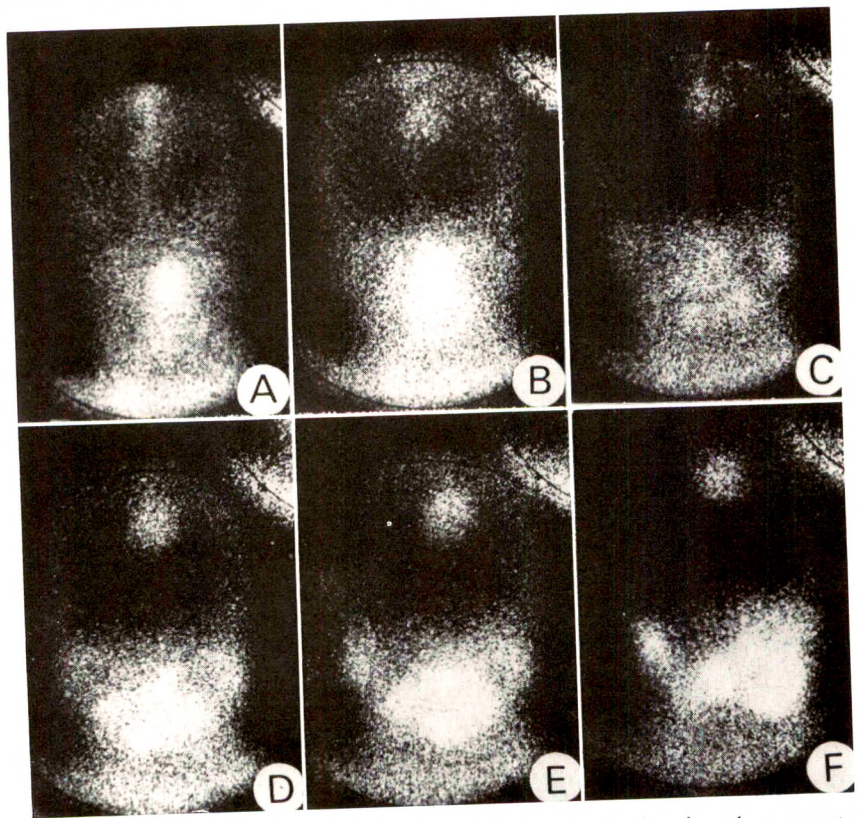


FIG. 8. Tc^{99m} serial scans of metastatic carcinoma in the left parasagittal region. Anteroposterior view. (*A*) 0–1, (*B*) 5–6, (*C*) 30–31, (*D*) 60–61, (*E*) 90–91, and (*F*) 120–121 minutes after the intravenous injection of 10 mc of Tc^{99m}.

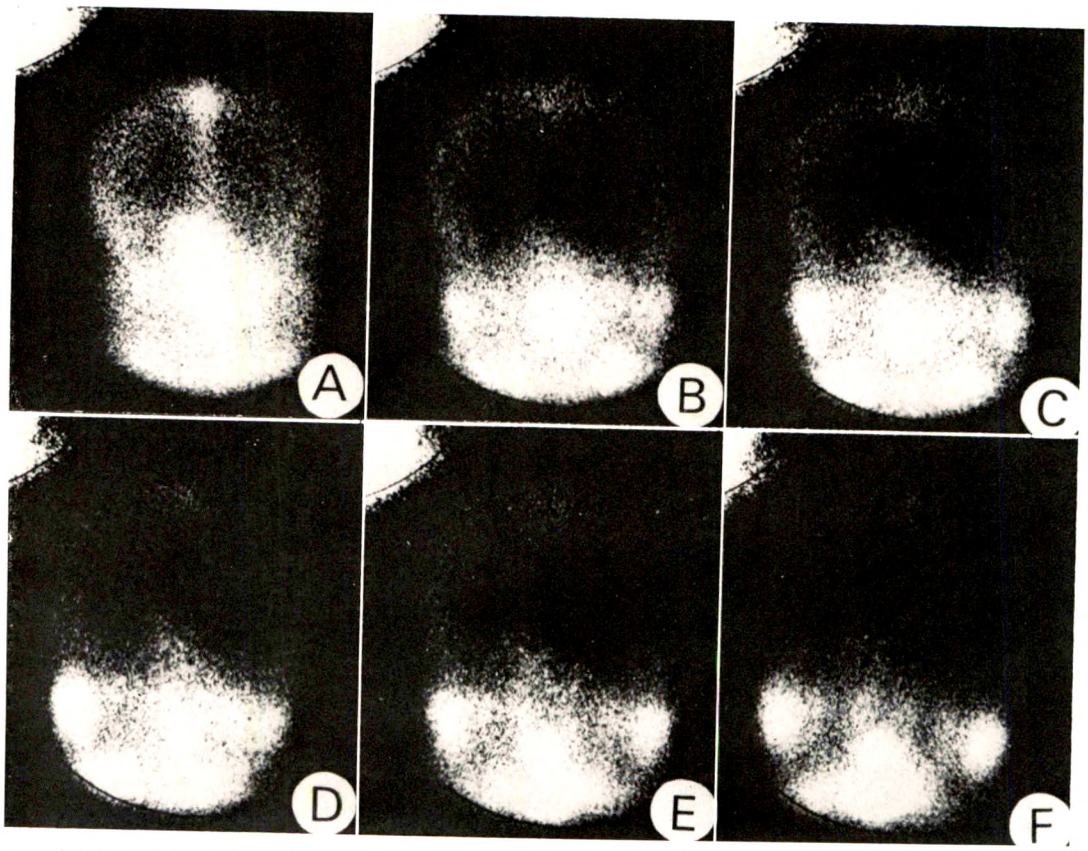


FIG. 9. Tc^{99m} serial scans of ethmoid cell cancer extending intracranially. The initial high radioactivity in the focus decreased with time. (*A*) 0–1, (*B*) 15–16, (*C*) 30–31, (*D*) 45–46, (*E*) 60–61, and (*F*) 120–121 minutes after the intravenous injection of 10 mc of Tc^{99m}.

jection, and the wash-out was slower in the focus than in the surrounding normal brain. MAA-I^{131} scans also demonstrated the focus to be low in radioactivity.

Figure 15, *A-D* is an example of Xe^{133} serial scanning in another case of right frontal cystic tumor. The focus remained cold during the serial scannings with Tc^{99m}. Carotid angiograms showed an avascular, cystic mass. A cold focus in the Xe^{133} scans also supported the diagnosis of cystic tumor, which was verified later by operation.

In the case of a highly vascularized oligodendroglioma illustrated in Figure 10, *A-F*, the uptake of Tc^{99m} showed a regressive and not progressive accumulation of radioactivity as described previously. Accumulation of a large amount of MAA-I^{131} in the tumor was in good agreement with the Tc^{99m} scan pattern as well as the angiographic findings. The considerable radioactivity noted in the lung also supported the angiographic demonstration of arteriovenous fistulas in the tumor.

DISCUSSION

It has been reported by several authors that the morphologic and chronologic patterns of isotope uptake differ from one type of lesion to another.

Schlesinger, DeBoves and Taveras[10] reported the results of repeat brain scanning with RISA-I^{131}. Lesions with abundant blood supply and unique hypervascularity, such as arteriovenous anomalies and angioblastic meningiomas, were best seen immediately after injection. Meningiomas generally appeared by 24 hours after injection and were most vivid within this period, whereas gliomas appeared at 24 hours but became more obvious by 48 hours. Avascu-

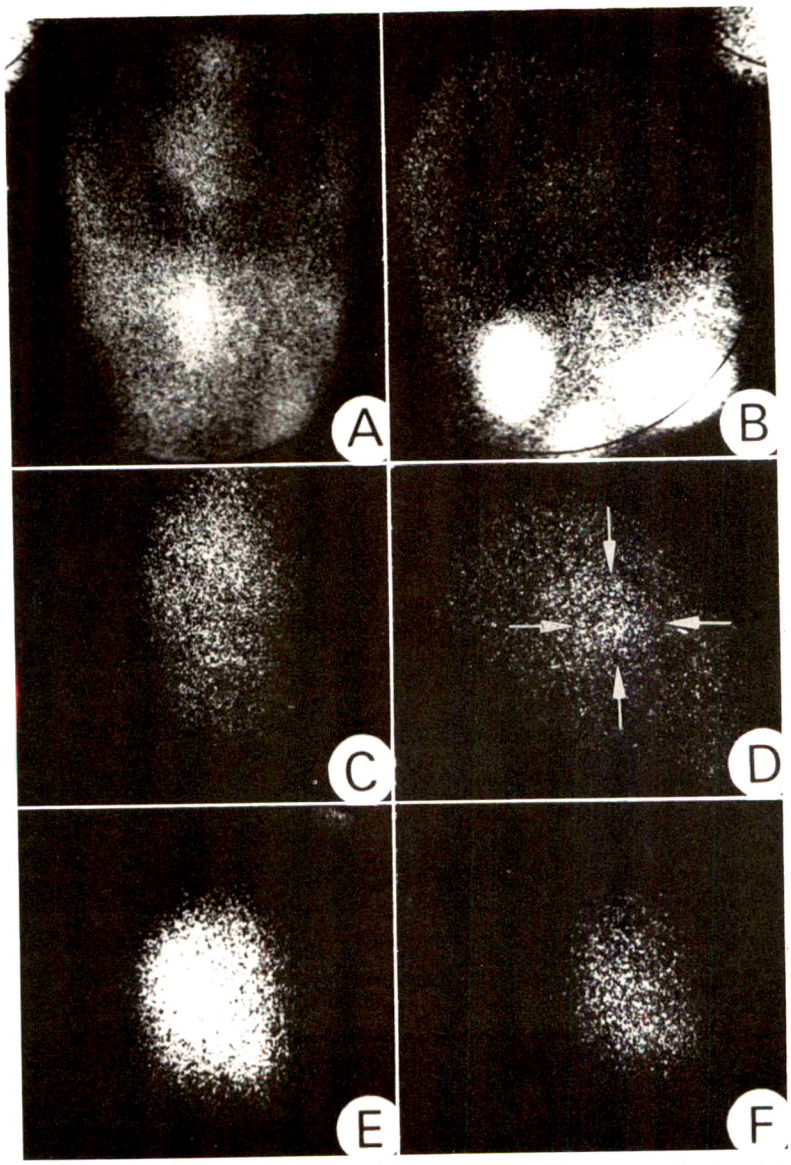


FIG. 10. Highly vascular oligodendroglioma. (*A*) Anteroposterior and (*B*) right lateral views of a Tc^{99m} scan depict the hot focus. (*C*) Anteroposterior and (*D*) right lateral views after the intracarotid injection of 100 μc of MAA-I^{131} show the rich vascularity of the tumor (arrows in *D*). (*E*) 0–30 second and (*F*) 75–105 second scintiphotographs after the intracarotid injection of 10 mc of Xe^{133}. Rapid washout suggests high tumor blood flow. Tc^{99m} serial scanning showed a regressive accumulation of radioactivity.

lar astrocytomas were poorly demonstrated, and cystic lesions began to appear in the late scan series and were best delineated after 48 hours. Budabin[1] also stressed the importance of early scanning in arteriovenous malformations using either RISA-I^{131} or chlormerodrin-Hg^{197} as tracers.

Based on the numerical data obtained with RISA-I^{131}, Planiol[5] classified the radioactive foci into 4 main categories. The early and clear focus corresponded to a meningioma in 74 per cent of the cases. In the delayed and blurred focus, 63 per cent were glioblastomas and 62 per cent were astrocytomas, whereas 71 per cent of metastatic lesions showed the delayed and clear focus. The early and blurred type was the

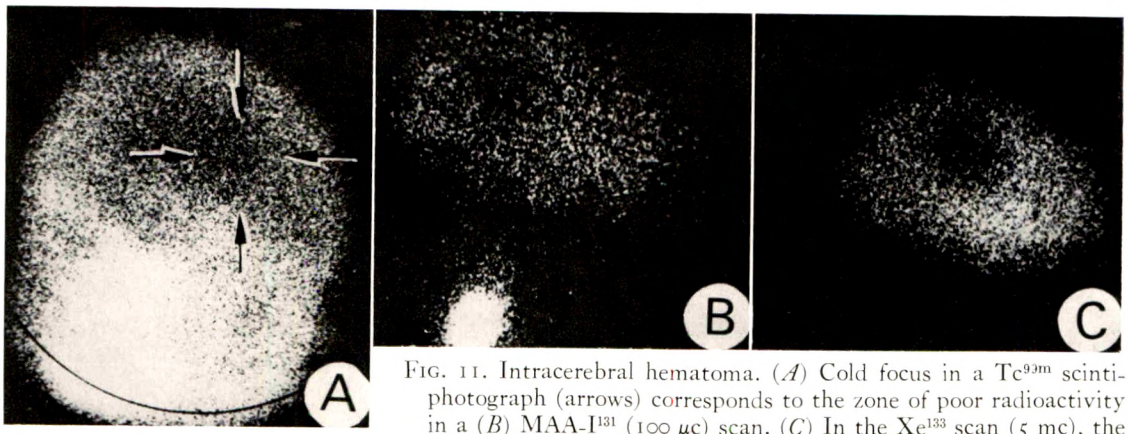


Fig. 11. Intracerebral hematoma. (*A*) Cold focus in a Tc^{99m} scintiphotograph (arrows) corresponds to the zone of poor radioactivity in a (*B*) MAA-I^{131} (100 μc) scan. (*C*) In the Xe^{133} scan (5 mc), the focus was cold during injection and the washout was slow. These results suggest that the focus is poor in vascularity and blood flow.

least frequently seen, and was found mostly in gliomas.

Economos and co-workers[2] described the results of serial scanning with chlormerodrin-Hg^{203} or Hg^{197}. In meningiomas, the maximum uptake occurred early; *i.e.*, 1–2 hours after injection. After this the foci lost their activity progressively and more or less rapidly. Gliomas could produce the early foci, but their uptake increased with time, and the foci often remained clear for 24 hours or more. Abscesses, infarctions and intracerebral hematomas also showed a progressive increase in radioactivity, but the uptake was much lower than in the gliomas.

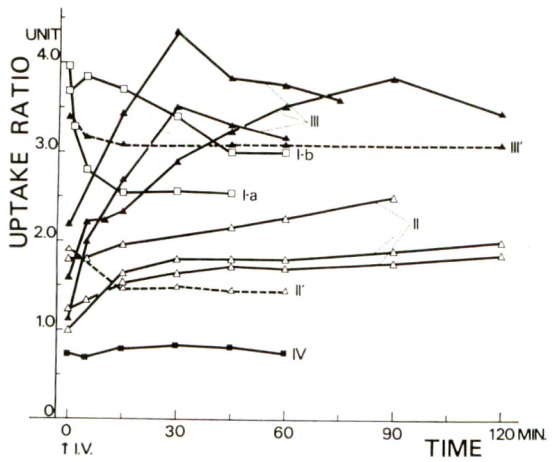


Fig. 12. Characteristic samples of uptake ratio patterns: I-a. Arteriovenous malformation. I-b. Meningioma. II. Oligodendroglioma, astrocytoma and cerebral infarction. III. Glioblastoma, carcinoma and sarcoma. IV. Intracerebral hematoma. II′ represents an atypical case of oligodendroglioma (Fig. 10, *A-F*), and III′ an unusual case of carcinoma, both of which showed a regressive pattern of uptake.

Our results with Tc^{99m} serial scanning compare favorably with these previous studies. The uptake of Tc^{99m} may be either progressive or regressive. The regressive course of accumulation was observed most often in arteriovenous malformations, meningiomas and cavernous angioma. Few cases of glioma and metastatic carcinoma showed the regressive pattern. In contrast, gliomas, metastatic carcinomas, sarcomas, abscesses and cerebral infarction showed the progressive accumulation of radioactivity. The intracerebral hematomas and cysts comprised another type of lesion and demonstrated a persistently cold focus.

When the uptake ratios were determined by use of the 1,600 channel analyzer, however, the chronologic course of uptake seemed to differ in arteriovenous malformations from meningiomas. In arteriovenous anomalies, the uptake ratio was maximum immediately after injection, whereas in the majority of meningiomas, the maximum uptake was reached 5 to 15 minutes later. Similarly, the lesions which showed progressive accumulation of radioactivity in serial scintiphotographs also ex-

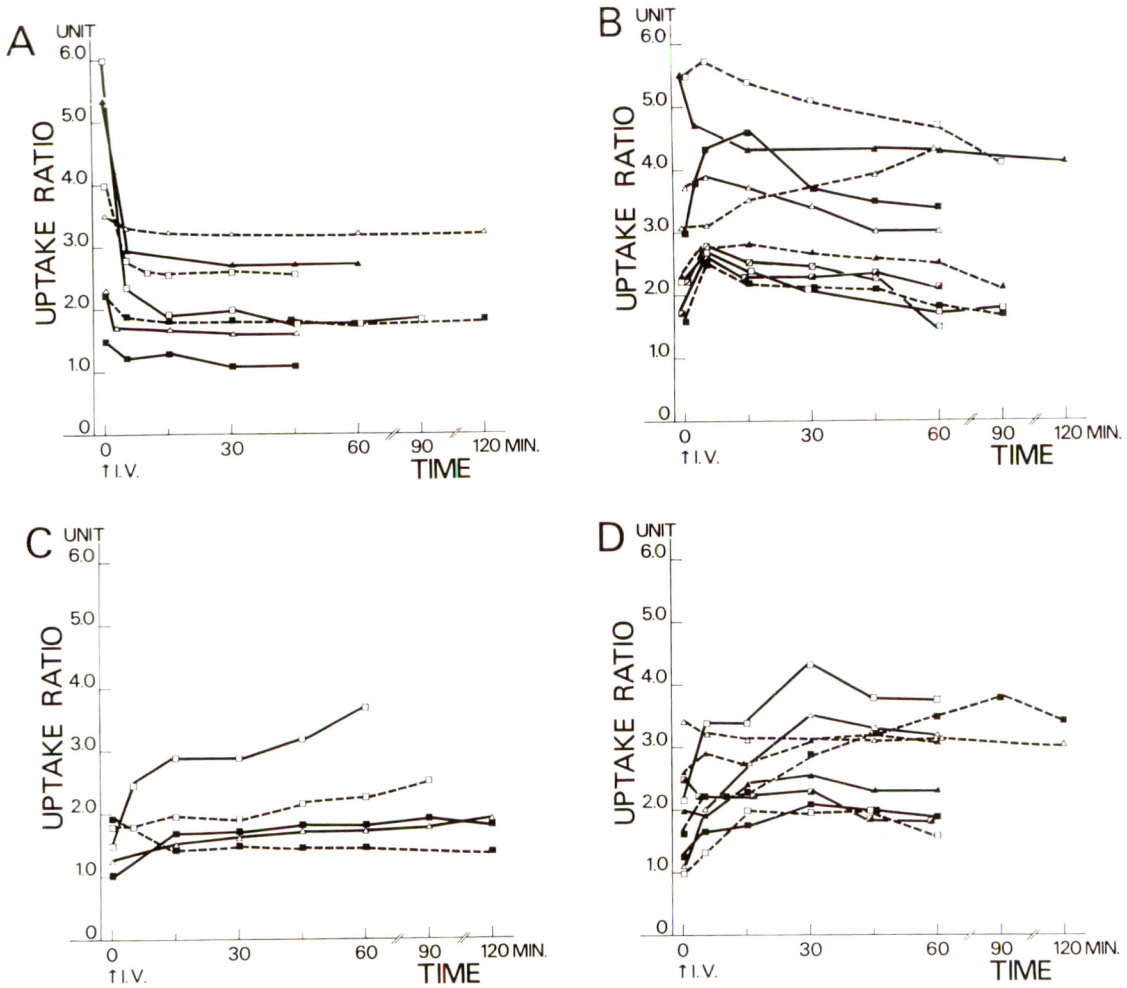


FIG. 13. Diagrams showing the uptake curve in: (*A*) Arteriovenous malformations, (*B*) meningiomas and cavernous angioma, (*C*) astrocytomas, oligodendrogliomas and cerebral infarction, and (*D*) glioblastomas, carcinomas and sarcomas.

hibited different behaviors. In one group the uptake ratio was low initially and increased steadily or reached the plateau during the period of study, but it never decreased. In the other group, the uptake ratio, after reaching the highest value in 30–45 minutes after injection, showed a gradual decrease, although the ratio at the end of the study remained still higher than the initial value. Persistently cold foci comprised the last group in which the uptake ratio never exceeded the unit.

Since no case of arteriovenous malformation in the present series had a recent hemorrhage or seizures, it seems apparent that the radioactivity in the focus is mainly due to a large quantity of blood pool in the anomalous vessels. Meningiomas and cavernous angioma demonstrated the typical tumor vasculature on the angiograms, and the Xe^{133} scan clearly showed the increased tumor blood flow. A large amount of MAA-I^{131} was entrapped in the tumor, and in several cases lung scanning also proved the existence of arteriovenous shunts. In the exceptional cases of glioma and metastatic lesion which showed regressive patterns of uptake, carotid angiography demonstrated tumors with extremely high vascularity. Xe^{133} and MAA-I^{131} studies also suggested

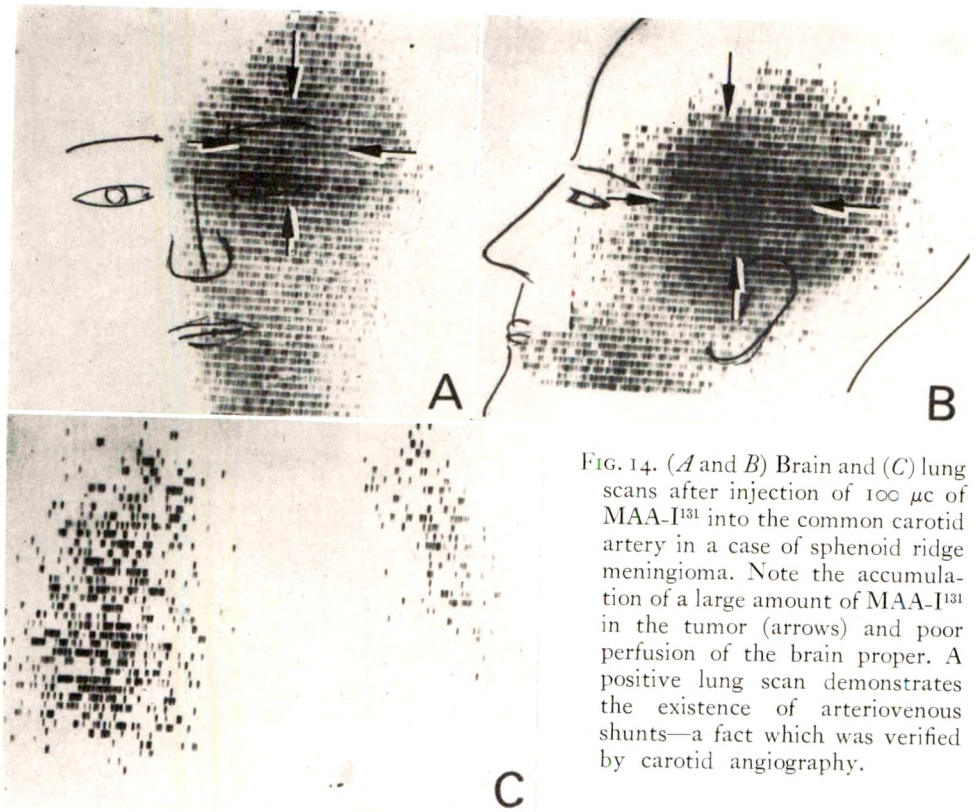


Fig. 14. (*A* and *B*) Brain and (*C*) lung scans after injection of 100 μc of MAA-I^{131} into the common carotid artery in a case of sphenoid ridge meningioma. Note the accumulation of a large amount of MAA-I^{131} in the tumor (arrows) and poor perfusion of the brain proper. A positive lung scan demonstrates the existence of arteriovenous shunts—a fact which was verified by carotid angiography.

the increased blood flow and a large vascular bed with or without arteriovenous shunts in the tumor. It seems plausible, therefore, that the regressive pattern of uptake depends primarily on the increased blood pool in the focus and not necessarily on the pathology of the lesion itself. In cases where the large blood pool is the main, if not the only, mechanism of radioactivity, then the chronologic course should follow the pattern of arteriovenous anomalies (Group I-a), as has been suggested by Budabin.[1] In most of the meningiomas and other highly vascularized tumors, however, there seems to exist another additional mechanism of isotope uptake, which modifies the uptake curve in a varying degree (Group I-b).

In the Group II foci with progressive accumulation of radioactivity increased blood pool does not seem to play any significant role in the isotope uptake. Tumor stain was never observed on angiograms; instead, the focus tended to be avascular. Xe^{133} and MAA-I^{131} studies also supported this finding. In this group of lesions, local breakdown or lack of a barrier mechanism might be the main factor responsible for progressive accumulation of Tc^{99m}; however, this remains to be studied further.

One case of cerebral infarction is of special interest in that the central focus showed a typical progressive uptake, whereas the perifocal hyperemic zone already was impregnated in the early scintiphotographs (Fig. 6, *A-F*). The central softened focus and richly perfused perifocal area had apparently separate and independent mechanisms for isotope uptake.

The results of Xe^{133} and MAA-I^{131} scanning were less uniform in Group III focus, but the lesions which showed the focal accumulation of MAA-I^{131} and a rapid clearance of Xe^{133} also demonstrated a high degree of tumor vasculature on angiography. The uptake of Tc^{99m} resembles that in Group II; however, the secondary decrease in uptake which is characteristic of

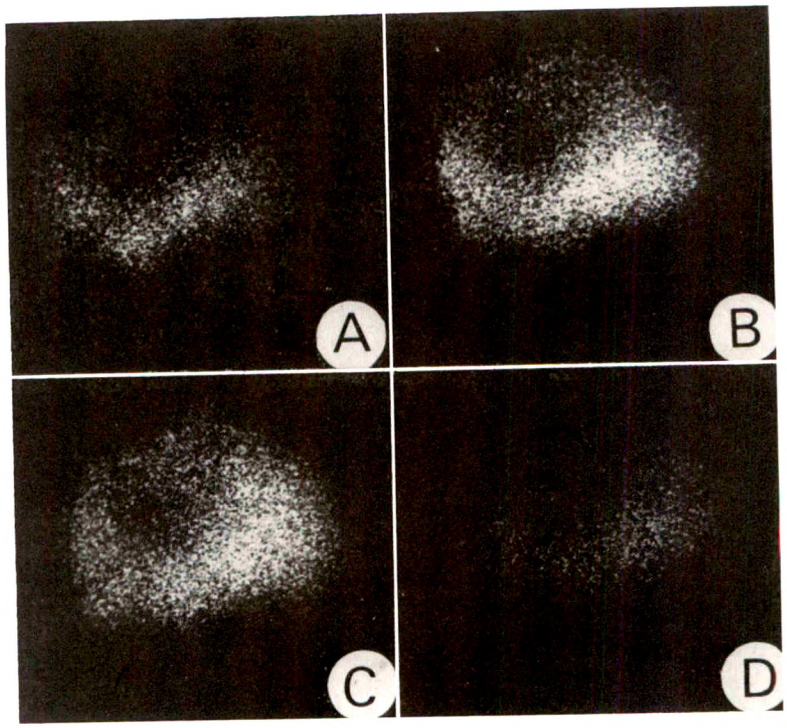


Fig. 15. Xe^{133} scans in a case of cystic tumor in the right frontal lobe. Low blood flow in the focus was suggested by the cold focus during injection of 10 mc of Xe^{133} (*A*) and slow washout thereafter. (*B*) 75–105, (*C*) 150–180, and (*D*) 225–255 second scintiphotographs.

this group may be due to the vascular factor. It is interesting to note that the lesions which showed the uptake pattern of initial increase followed by decrease were malignant tumors without a single exception.

In Group IV lesions, Xe^{133} and MAA-I^{131} studies clearly showed the decreased blood flow and vascular bed in the focus, and in Tc^{99m} scanning the uptake ratio remained less than a unit. All these scan data suggested that the focus should be avascular, and this was confirmed later by angiography and surgery.

Thus, it is concluded from the present study that the vascularity and blood flow in the focus are the important factors in determining the time course of uptake in Tc^{99m} serial scanning. A more precise prediction of tumor pathology seems to be possible when the morphologic characteristics of the focus are combined with the time course of the isotope uptake in analyzing the scan data. The use of computer analysis seems to be promising.

SUMMARY

1. Serial brain scanning with gamma-ray scintillation camera and Tc^{99m} pertechnetate was performed and the chronologic patterns of serial scintiphotographs were related to the pathology.

Regressive accumulation of radioactivity of the focus was observed in arteriovenous anomalies, meningiomas and angioma, whereas the gliomas, metastatic carcinomas, sarcomas, infarctions and abscesses showed a progressive course of isotope uptake. In intracerebral hematomas and cystic tumors the focus remained persistently cold.

2. Chronologic patterns of the uptake ratio were determined digitally and classified into 4 groups. In Group I, the uptake ratio was maximum immediately or shortly after injection and then decreased rapidly.

In Group II the uptake ratio showed a gradual increase. In Group III, an initial increase was followed by a decrease, and in Group IV, the uptake ratio remained below 1.0.

3. Xe^{133} and MAA-I^{131} scanning data showed that the Group I lesions were rich in vascular bed and had a high blood flow in the focus. Group II and IV lesions were avascular and Group III foci showed a less uniform vascular pattern.

4. It is concluded that the tumor vascularity plays an important role in determining the regressive course of uptake of Tc^{99m}. Another mechanism of isotope uptake, presumably local breakdown or lack of barrier mechanisms, seems to be the main factor in Group II and III uptake patterns.

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ISOTOPE ENCEPHALOGRAPHY WITH CHOLOGRAFIN I^{131}

BIOLOGIC AND PHYSICAL CHARACTERISTICS

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ISOTOPE encephalography combines diagnostic accuracy and safety, while causing little discomfort to the patient.

Many agents have been utilized in isotope encephalography but relatively little has been known on their distribution *in vivo* and of their relative efficiency in detecting brain abnormalities.

Early experience in this matter was accumulated by Moore[9] in 1948 when he used diiodofluorescein I^{131} during a craniotomy to determine the extent of the lesion. Ashkenazy and Crawley[1] confirmed the uptake of an isotope by the tumor using R.I.S.A. I^{131} (radioiodinated serum albumin I^{131}) and an external point-counting technique. DiChiro[4] used R.I.S.A. I^{131} for brain scanning in 1961.

In 1962 Blau and Bender[2] reported that chlormerodrin Hg^{203} has a high affinity for brain tumors. This material delivers a relatively high renal radiation dose. Sodee[12] in 1963 compared chlormerodrin Hg^{203} with chlormerodrin Hg^{197} and proved that the latter produces brain scans of good quality, decreasing the radiation exposure by a factor of approximately 8.

Currently technetium 99m is used for brain scanning. Its short half-life and lack of particulate radiation result in a low radiation dose to the patient. It may be administered orally or intravenously. After intravenous administration, the radiation dose to the large bowel amounts to 1.0–1.5 rads,[11] and 0.4 rads are delivered to the stomach.[8] Oral administration causes an increase of the dose delivered to the large bowel to 2.1 rads.[7]

The search for an ideal scanning agent continues. DiChiro[4] defined the desirable qualities of such material. The agent should: (1) indicate the presence of the lesion; (2) locate the site of the lesion; (3) define the extent of the lesion; (4) point to the nature of the lesion; and (5) entail minimal hazard and discomfort to the patient.

To fulfill these criteria the material used for scanning should have the following properties:[8]

(a) Gamma energy of the nuclide should be between 0.1 and 0.5 mev. With energies higher than 0.5 mev., satisfactory collimation becomes difficult.
(b) There must be a high concentration of the material in the tumor and a relatively low concentration in the surrounding brain and the scalp.
(c) The material should not concentrate selectively in any organ to an extent that it creates a radiation hazard.
(d) The material should have a short effective half-life.

Such an agent has not yet been found.

MATERIAL AND METHODS

The purpose of this study was to compare chologrefin I^{131} (iodipamide I^{131}) with technetium 99m, chlormerodrin Hg^{203} and R.I.S.A. I^{131}. We chose chologrefin I^{131} as the scanning agent because it fulfilled the criteria mentioned above, except for the fact that it is concentrated and excreted almost entirely by the liver. Reports in the literature of the short effective half-life

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caused us to believe that doses in the order of 1.0–2.0 mc could be safely administered, thus minimizing the radiation exposure compared with chlormerodrin Hg^{203} and R.I.S.A. I^{131}. We evaluated the diagnostic quality of scans obtained with these 4 agents and related the value of the obtained information to the radiation dose delivered by the agent to the patient.

Sixty-three patients had scannings with cholografin I^{131} and 1 of the other 3 agents. Initially, cholografin I^{131} scannings were performed first and followed in 4 to 10 days by the scannings utilizing the other radioactive medium. During the final period of the study, chlormerodrin Hg^{203} and technetium 99m scannings were followed by cholografin I^{131} scanning 1 or 2 days later. All 4 radioactive media were injected intravenously; the dosage for cholografin I^{131} was 1.0 to 2.0 mc, for R.I.S.A. I^{131} 0.5 mc, for chlormerodrin Hg^{203} 0.6–0.8 mc, and for technetium 99m 10.0 mc.

The cholografin I^{131} scannings were performed at 4 hours, 12 hours, 24 hours, 48 hours and 72 hours after injection. After experience with a few patients we discontinued the scannings performed at 48 and 72 hours because their diagnostic quality was not satisfactory due to the low remaining radioactivity in the brain.

Blood was drawn at 5, 10, 30, 60 minutes, and 2, 4, 6, 12, 24, 48 and 72 hours after injection. The blood samples were counted in a well-counter to determine the effective half-life. Serum specimens obtained from patients injected with cholografin I^{131} were passed through an amberlite I.R.A. 400 anion exchange resin to determine the amount of cholografin I^{131} which passed through the column.

The serum of 2 patients previously injected with cholografin I^{131} was electrophoresed on paper strips which subsequently were cut into zones corresponding to the serum protein fractions. The individual zones were counted in a gamma well-detector.

Counts were obtained over the tumor, when it was well delineated, and over the normal brain in the corresponding area in the opposite hemisphere, as well as over the liver, thyroid, left thigh and left shoulder.

The scannings utilizing R.I.S.A. I^{131} were performed 24 and 48 hours after injection. Patients in which chlormerodrin Hg^{203} was used as a scanning agent were scanned 1 to 4 hours and 24 hours after injection, and patients with technetium 99m were scanned immediately after the injection. For purposes of comparison, all scannings on the same patient were performed with the same photoscanner. Three physicians evaluated each of the scans independently.

One of our first patients demonstrated markedly increased counts over the thyroid gland after cholografin I^{131} administration. Thereafter, Lugol's solution was administered 24 hours prior to the injection of cholografin I^{131}.

RESULTS

Cholografin I^{131} was added to normal serum *in vitro* and passed through an amberlite I.R.A. 400 anion exchange resin. Forty to 65 per cent of the radioactivity was repeatedly recovered in the effluent. When cholografin I^{131} alone was passed through such a column less than 5 per cent was recovered in the effluent. Serum specimens from 6 patients obtained up to 24 hours after the intravenous administration of cholografin I^{131} were passed through the anion exchange resin columns. As little as 45 and as much as 99 per cent of the radioactivity in the serum sample was recovered in the effluent; the interval of time after injection did not appear to influence the result.

The serum of 2 patients previously injected with cholografin I^{131} was electrophoresed and the paper strips cut into zones corresponding to the serum protein fractions. The individual zones were counted in a gamma well-detector. Radioactivity was found in association with all major serum protein fractions, and 35 per cent of the total radioactivity was in the albumin zone. These findings are interpreted to indicate protein binding of the cholografin

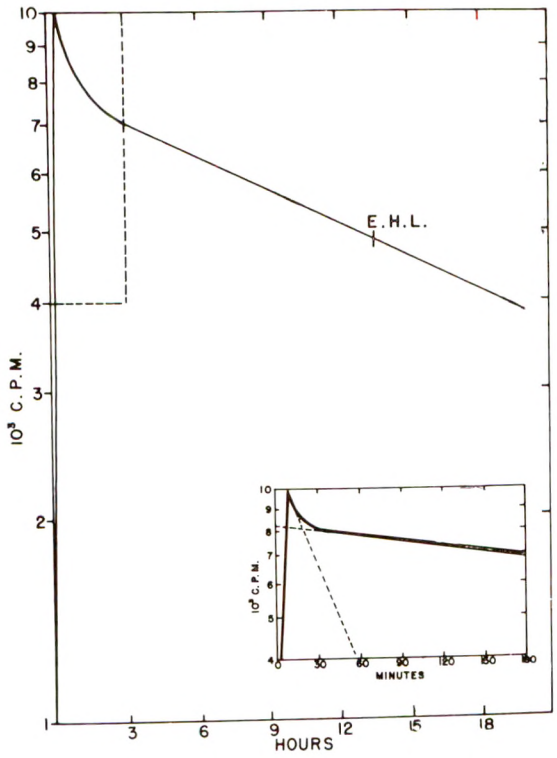


FIG. 1. Curve demonstrating the effective half-life (E.H.L.) of chlografin I^{131} in man. *Insert.* Portion of the curve within the dotted area for better visualization of the rapid and slow excretion phases.

I^{131} *in vitro* and *in vivo*.

The effective half-life (E.H.L.) of chlografin I^{131} in the liver, as reported in the literature, varies from 2 to 9 hours. Our experiments revealed that the transit of chlografin I^{131} through the normal liver consisted of 3 phases as described in previously published results:[8] an initial accumulation phase of 5–15 minutes duration; a rapid excretory phase with an effective half-life of 45–150 minutes; and a slow excretory phase with an effective half-life of 18–24 hours. The combined effective half-life of disappearance from the normal liver varied from 12–15 hours (Fig. 1). In patients with liver disease, the disappearance of chlografin I^{131} from the liver was slower and directly related to the severity of the liver disease, as measured by standard laboratory liver function tests.

MacIntyre *et al.*[6] and Fischer[5] indicated that the difference in reported E.H.L.s of chlografin I^{131} is dependent upon the dose, possibly due to the dual excretory routes. The major excretory route is usually via the bile passages, the secondary route being the urinary tract. In 1 patient with liver metastases we injected 10 μc of chlografin I^{131} and determined the E.H.L. in the liver to be 32 hours. Forty-eight hours later we injected 20 cc. of nonradioactive chlografin followed by an additional 20 μc of chlografin I^{131}. The E.H.L. in the liver was again determined (Fig. 2). The maximum accumulation of radioactive material within the liver was delayed for 24 hours and was somewhat smaller than that obtained without loading when corrected for the amounts of radioactive material injected. Also the E.H.L. was changed from 34 hours to 24 hours. This may be explained on the basis that the loading dose exceeded the maximum hepatic capacity, resulting in higher blood levels of radioactivity, which probably exceeded the renal threshold as proposed by MacIntyre *et al.*[6] and inferred by Fischer.[5]

In 6 patients the tumor-to-brain ratio was obtained early (2–4 hours) and late (approximately 24 hours) after the administration of the scanning agent chlografin I^{131} and chlormerodrin Hg^{203}. The early tumor-to-brain ratio averaged 1.8 for chlografin I^{131} and 2.1 for chlormerodrin Hg^{203};

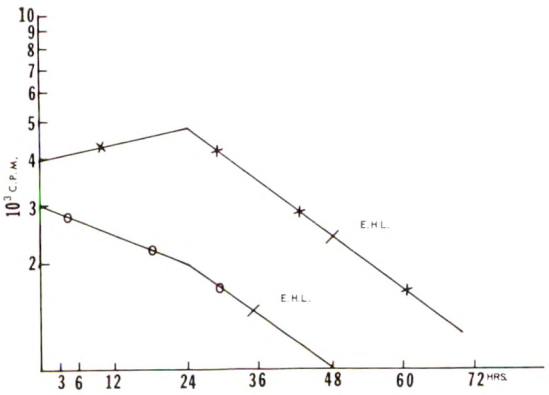


FIG. 2. Curves demonstrating the E.H.L. of chlografin I^{131} in a patient with hepatic metastases (O), and the blocking effect of nonradioactive chlografin (X).

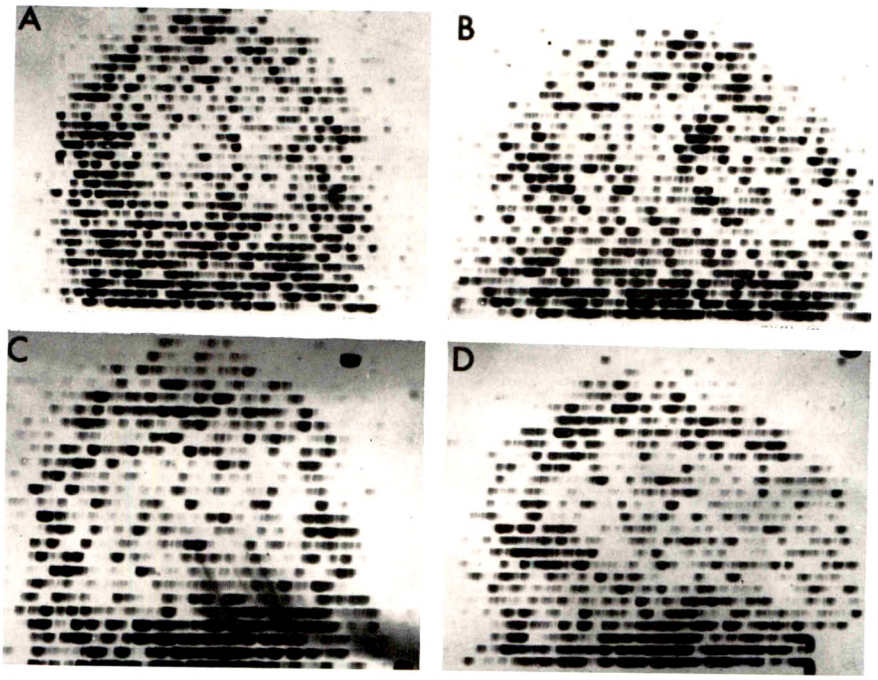


FIG. 3. (*A*) Frontal and (*B*) right lateral projections of cholografin I^{131} encephalogram (4 hour study) of a recurrent astrocytoma of the right frontoparietal region. (*C* and *D*) Comparable R.I.S.A. I^{131} projections (24 hour study). The cholografin I^{131} scan is superior to the R.I.S.A. I^{131} scan.

the late ratio was 1.8 and 1.9, respectively.

In all cases the cholografin I^{131} scans visualized lesions demonstrated by the other 3 radioactive media. In many cases the cholografin I^{131} visualization of the tumor was superior to scans obtained with chlormerodrin Hg^{203} and R.I.S.A. I^{131} (Fig. 3, *A–D*; and 4, *A–D*). On some occasions the 24 hour cholografin I^{131} scan showed the lesion to better advantage than the 4 hour scan. In Figure 5, *E* and *F* a case is shown where the 24 hour cholografin I^{131} scan displayed the true extent of a frontal sinus tumor invading the frontal lobe of the brain. Both the technetium 99m and the 4 hour cholografin I^{131} scans revealed the lesion (Fig. 5, *A–D*), but not in its true extent as determined by other studies.

In some cases, especially in patients with a prolonged E.H.L. due to liver disease, the graphic demonstration of the lesion by cholografin I^{131} was superior to that revealed by the other radioactive media.

DISCUSSION

The advantage of cholografin I^{131} and R.I.S.A. I^{131} as scanning media when compared with chlormerodrin Hg^{203} and technetium 99m lies in the fact that, if desired, scanning can be repeated without reinjection up to 24 hours with cholografin I^{131} and up to 48 hours with R.I.S.A. I^{131}.

As previously mentioned, most of the cholografin I^{131} is eliminated via the bile passages and finally the intestinal tract. The dose delivered to the intestines, especially to the large bowel wall by beta particles, was estimated by MacIntyre *et al.*,[6] on the basis of Loevinger's[10] analysis for beta particle slab of infinite thickness, as not to exceed 6 millirads per hour at the distance of 1 mm. from the surface. The contribution of gamma radiation to the same site was 20 millirads per hour.

The total ovarian exposure (as calculated by Comas and Brucer[3]) due to the passage of I^{131} through the bladder would amount to not more than 5 millirads for the estimated 300 μc which may be excreted by the kidneys. The dose to the left ovary from the contents of the sigmoid colon would be on the order of 2.7 millirads per hour. The

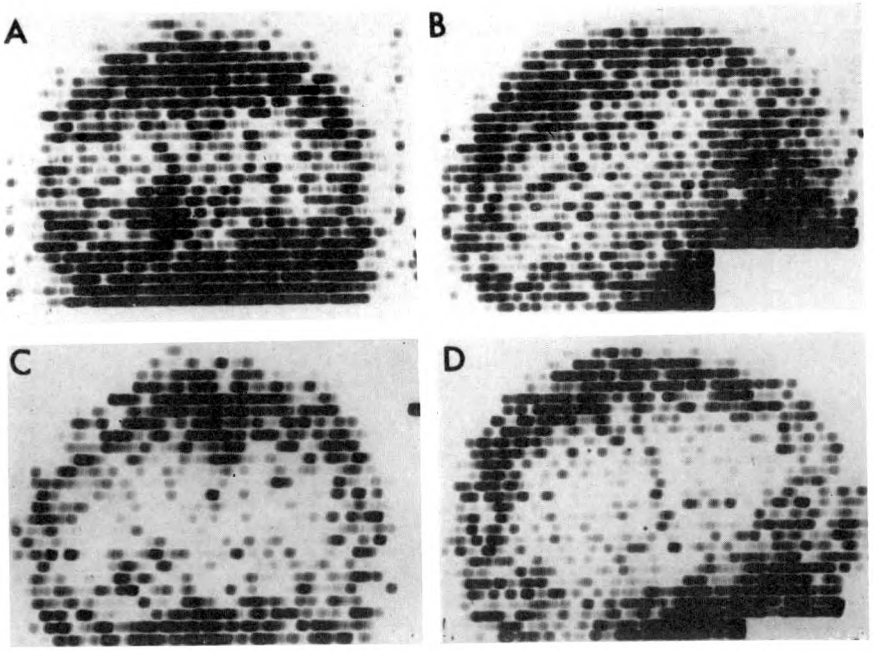


FIG. 4. (*A*) Frontal and (*B*) right lateral projections of the chlografin I^{131} encephalogram (4 hour study) which demonstrate metastatic ovarian carcinoma to the right frontal lobe. (*C* and *D*) Comparable projections with chlormerodrin Hg^{203} (4 hour study). The chlografin I^{131} scan defines the lesion more clearly.

radiation exposure to all organs except the liver could be considerably reduced by administration of cathartics prior to the intravenous injection of chlografin I^{131}.

We consider the liver the target organ when chlografin I^{131} is administered. The estimated total dose delivered by the beta and gamma radiation to the liver weighing 1,700 gm. amounts to 6.53 rads per mc. The total body beta plus gamma dose to an individual weighing 70 kg. is estimated at 184 millirads per mc.[10]

An important factor influencing the tumor-to-brain concentration ratios of radioactive compounds appears to be the degree of binding to plasma proteins; the tumor-to-brain ratio is greater with compounds which bind to plasma proteins. Chlografin binds loosely to albumin and other serum proteins *in vivo* and *in vitro*, and this probably accounts for the selective concentration of this agent in brain tumors. Because chlografin is loosely bound to the serum proteins, and excreted by the liver, its blood disappearance rate is much faster than I^{131} albumin, resulting in reduced whole body irradiation to the patient and potentially greater tumor-to-brain concentration ratios.

The improved delineation of lesions with chlografin I^{131} is not due to an improved tumor-to-brain ratio, but rather to improved counting statistics resulting from the injection of a larger dose of radioactive material. Although the average tumor-to-brain ratio is not remarkably different for early and late scans, there were individual instances in which the ratio was greater during the late scans, and the lesion was better visualized on the late scan.

Chlografin tagged with presently available I^{123}, with a physical half-life of 13 hours and monoenergetic gamma emission of 159 kev. could be utilized to even greater advantage in brain scanning.

SUMMARY

The effective half-life of chlografin I^{131} varied from patient to patient. In patients with normal liver tests it ranged from 14 to 18 hours. Patients who had abnormal liver function showed an increased effective half-life (E.H.L.) as long as 58 hours. Blocking the excretory routes by the intravenous in-

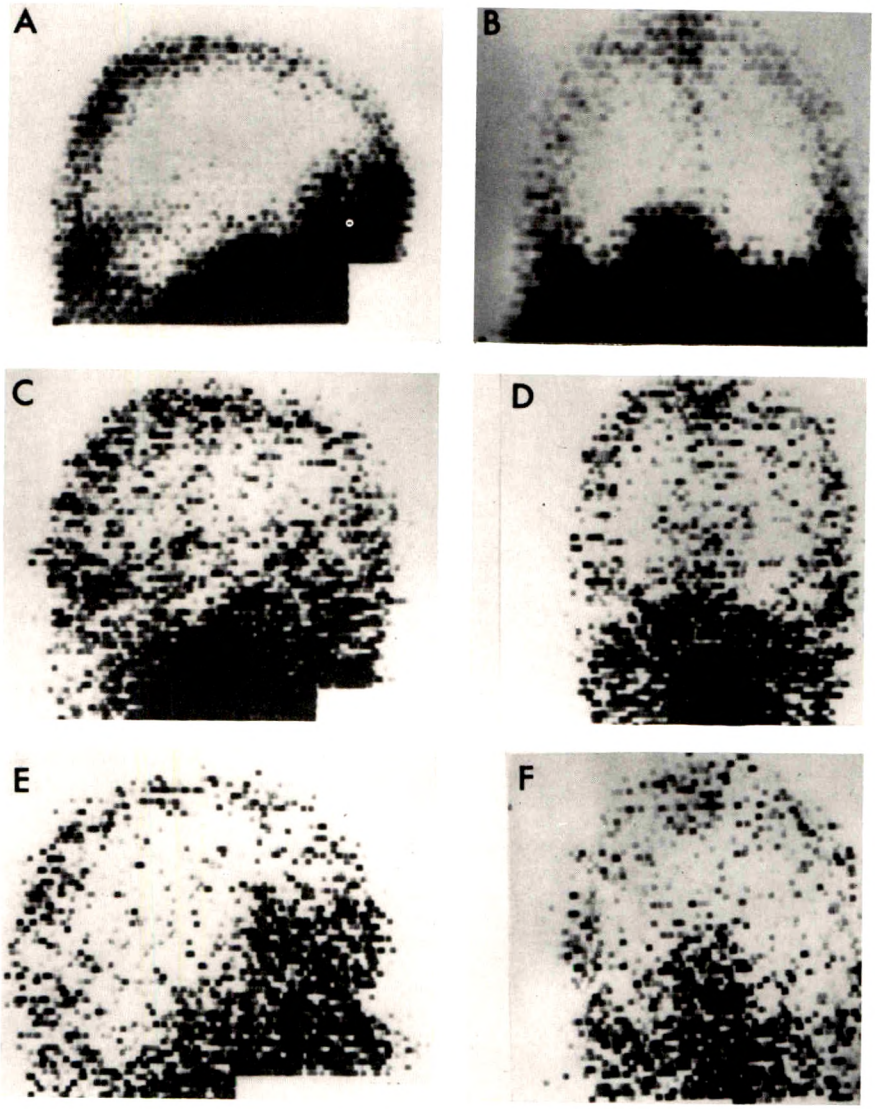


FIG. 5. (*A*, *C* and *E*) Right lateral and (*B*, *D* and *F*) frontal projections of an encephalogram of a patient with squamous cell carcinoma of the frontal sinus invading the anterior fossa. (*A* and *B*) Technetium 99m scans (15 minute study). (*C* and *D*) Cholografin I^{131} scans (4 hour study). (*E* and *F*) Cholografin I^{131} scans (24 hour study). The 24 hour cholografin I^{131} scan visualizes the lesion better than the other scans.

jection of 20 cc. of nonradioactive cholografin, followed by 20 μc of radioactive cholografin did not change the E.H.L. appreciably, but delayed the peak of concentration in the liver. Liver and renal functions as well as the amount injected determine the excretory pattern.

We found cholografin I^{131} a useful agent for brain scanning when compared with chlormerodrin Hg^{203}, R.I.S.A. I^{131} and technetium 99m. The whole-body irradiation burden compares favorably with chlormerodrin Hg^{203} and R.I.S.A. I^{131}. However, attention must be called to the fact that its dose is larger than that delivered by 10 mc of technetium 99m.

Evaluation of cholografin I^{123} as a scanning agent will be instituted in the near future.

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POSITIVE "BRAIN" SCANS IN FIBROUS DYSPLASIA AND OTHER LESIONS OF THE SKULL*

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WITH the widespread acceptance of brain scanning as a reliable procedure, several authors have reported positive scans in patients with lesions of the bony calvaria. While such reports were extremely rare during the era when radioactive iodinated serum albumin was the radionuclide of choice,[4] they have became more common with the advent of Hg^{203} and Hg^{197} chlormerodrin.[5,8] The use of Tc^{99m} sodium pertechnetate as a scanning agent has further increased the incidence of positive scans with lesions of the skull.[6,9,10,11] In addition, with this agent, vascular, inflammatory and neoplastic processes outside the cranium have also shown significant uptake.[1]

In the past 4 years, over 4,000 brain scannings have been performed at the University of Minnesota Hospitals utilizing Tc^{99m}. Fourteen patients with lesions of the bony calvaria had positive scans, the area of activity being closely correlated with the location of the lesions on roentgenograms of the skull. In a number of these cases, the scans were originally interpreted as showing intracranial pathology. It is the purpose of this communication, therefore, to emphasize that both benign and malignant lesions of the skull can produce areas of increased activity, that such scans can simulate the appearance of an intracranial process, and that the incidence of positive scans with lesions of the skull is more frequent with the use of Tc^{99m} as compared with mercury or iodine isotopes.

FIBROUS DYSPLASIA

In the past year and one-half, 3 patients with the roentgenographic picture of fibrous dysplasia of the skull have been evaluated at the University of Minnesota Hospitals. Two of these cases are biopsy proven. All 3 patients showed areas of considerable increased activity in the region of the lesion of the bony skull on Tc^{99m} brain scans.

Case I. L. O., U.M.H. 1067125. A 19 year old male college student first noted a hard nontender protuberant mass in the left parietal region 6 months prior to admission. Roentgenograms of the skull demonstrated a large relatively radiolucent lesion in the left parietal bone with a sclerotic margin (Fig. 1*A*). Tangential and tomographic views showed the lesion to be cystic in character and predominantly involving the outer table and diploë (Fig. 1, *B* and *C*). The inner table was intact, although displaced slightly medially. A brain scan utilizing 10 mc Tc^{99m} was obtained and showed a very sharply defined focus of increased activity in the identical region as the skull lesion (Fig. 1, *D* and *E*). Although the roentgenographic findings seemed most consistent with a diagnosis of fibrous dysplasia of the cystic type, the patient requested that the protuberant mass be removed. Histologic examination of the specimen showed bony spicules separated by narrow spaces filled with dense fibrous tissue and capillaries distended with erythrocytes, consistent with the diagnosis of fibrous dysplasia (Fig. 1*F*).

Case II. R.M., U.M.H. 972232. A 14 year old male was initially seen at the age of 5 years, at which time the parents had noted the presence of a mass in the right temporal region. The mass on examination appeared to extend into the frontal bone and the right orbit was smaller than its companion on the left and more low-set. There was a mild proptosis of the right eye.

Over the past 9 years, the mass has not changed in size or configuration. Roentgenograms revealed a dense sclerotic process involving and depressing the roof of the right orbit (Fig. 2, *A* and *B*). This markedly thickened ho-

* Presented at the Sixty-ninth Annual Meeting of the American Roentgen Ray Society, New Orleans, Louisiana, October 1–4, 1968.
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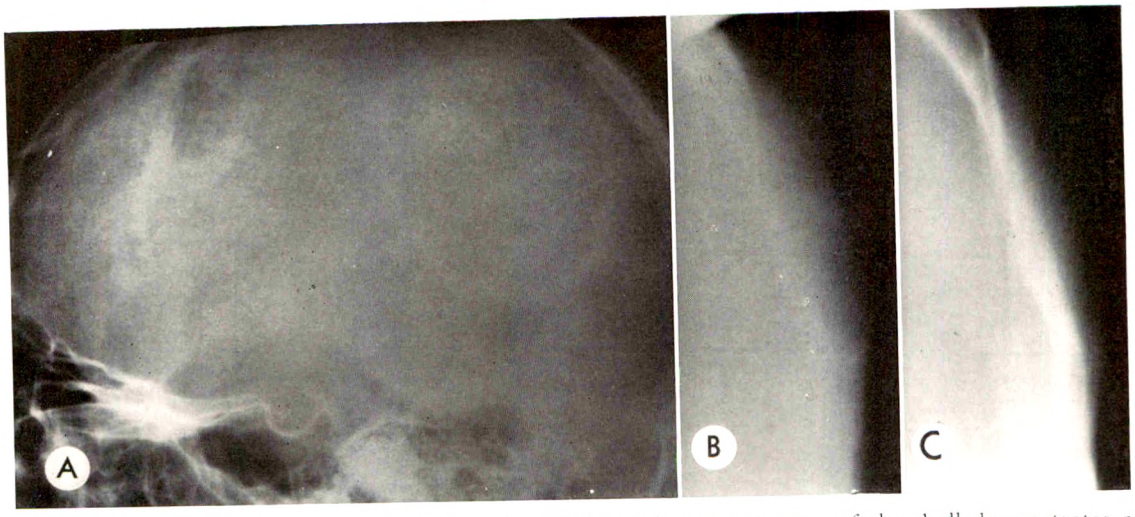


Fig. 1. Fibrous dysplasia in a 19 year old male. (*A*) Lateral roentgenogram of the skull demonstrates a cystic lesion of the parietal bone with a sclerotic margin. (*B*) Tangential roentgenogram and (*C*) tomogram show expansion involving the outer table and the diploë with thinning of the inner table.

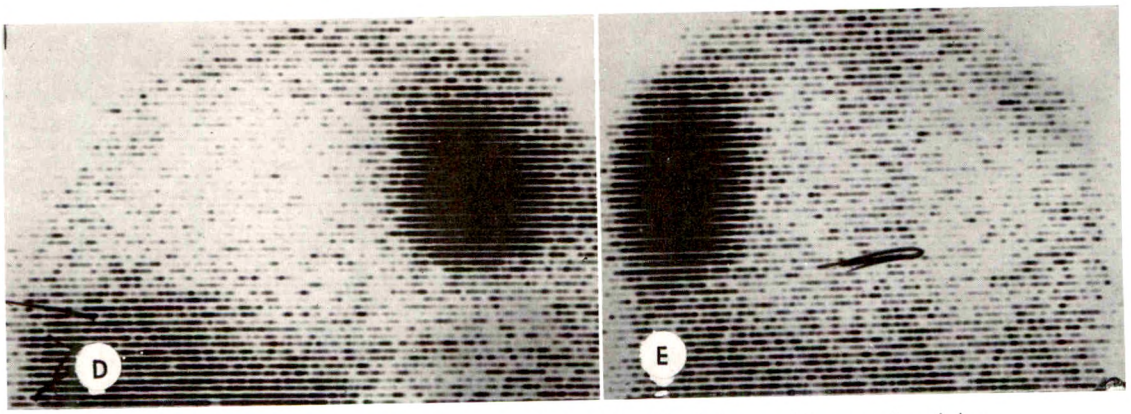


Fig. 1. (*D* and *E*) Tc^{99m} scans (10 mc) show localized focus of increased activity corresponding in location to the calvarial lesion.

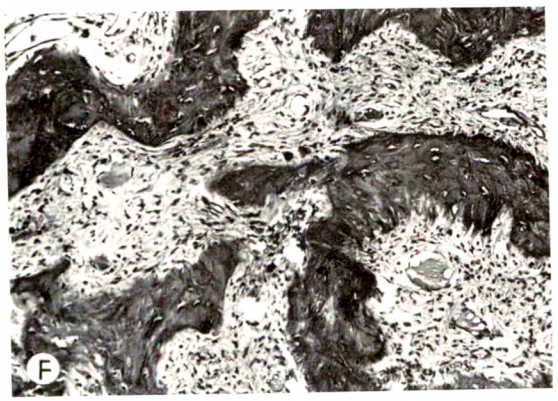


Fig. 1. (*F*) Microscopic section of the lesion shows dense vascular fibrous tissue between bony spicules, characteristic of fibrous dysplasia.

mogeneous bone extended medially into the body of the sphenoid and the posterior ethmoid cells. Both sphenoid wings were thickened on the right side. Carotid angiography revealed enlargement of the right ophthalmic artery which was displaced downward by the thickened orbital roof. The middle meningeal and other external carotid branches supplying the base of the skull anteriorly were also enlarged (Fig. 2*C*). Although this roentgenographic picture could have been produced by an extensive meningioma, later stages of the angiography failed to reveal any evidence for a tumor blush. There was slight displacement of the frontal branches of the anterior and middle cerebral arteries which was likely on the basis of the bone mass alone. A Tc^{99m} brain scan was obtained in 1968

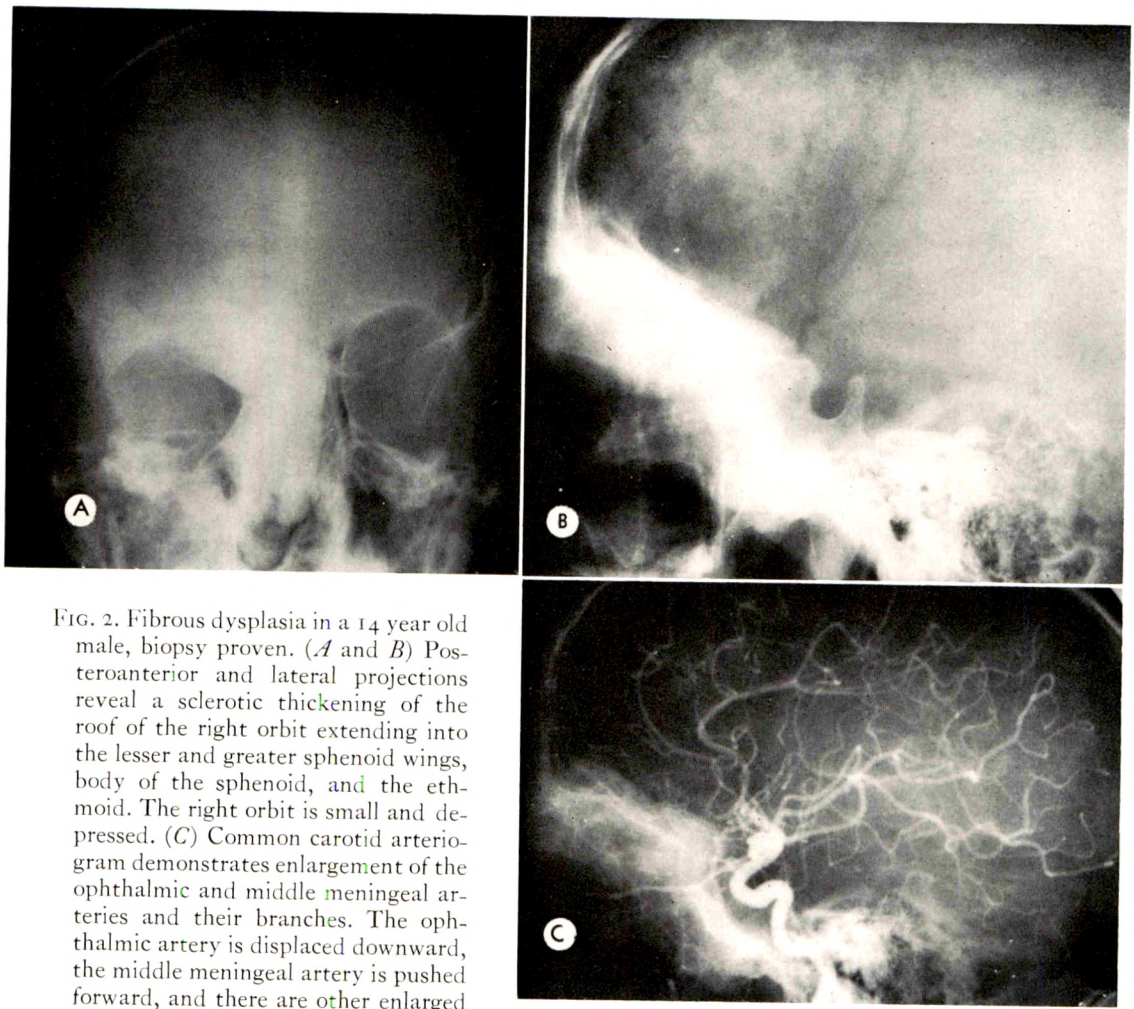


FIG. 2. Fibrous dysplasia in a 14 year old male, biopsy proven. (*A* and *B*) Posteroanterior and lateral projections reveal a sclerotic thickening of the roof of the right orbit extending into the lesser and greater sphenoid wings, body of the sphenoid, and the ethmoid. The right orbit is small and depressed. (*C*) Common carotid arteriogram demonstrates enlargement of the ophthalmic and middle meningeal arteries and their branches. The ophthalmic artery is displaced downward, the middle meningeal artery is pushed forward, and there are other enlarged branches of the internal maxillary artery which are also displaced forward by the thickened bone at the base of the skull anteriorly.

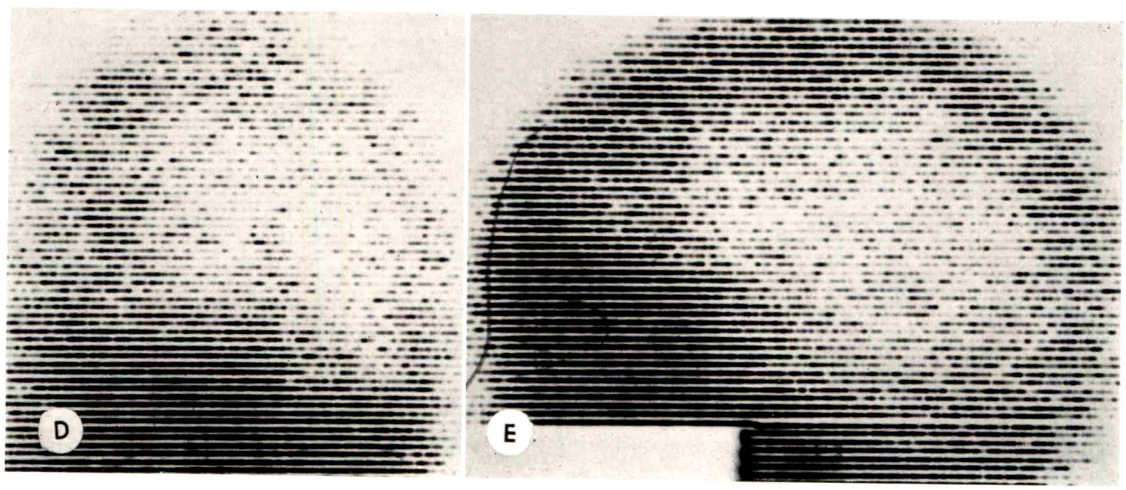


FIG. 2. (*D* and *E*) Tc^{99m} scans (10 mc) show area of increased activity in identical region as the lesion seen on the skull roentgenograms.

TABLE I

POSITIVE "BRAIN" SCANS IN LESIONS OF THE SKULL

	No. of Cases
Benign	
Fibrous dysplasia	3
Paget's disease	3
Histiocytosis X	2
Hemangioma	1
Malignant	
Metastatic carcinoma of breast	3
Metastatic neuroblastoma	1
Primary fibrosarcoma	1
Total	14

on this patient, now aged 14, and showed a large area of increased activity corresponding in location to the bone lesion seen on the roentgenogram (Fig. 2, *D* and *E*). Despite the considerable difference in roentgenographic appearance between this patient and the first case, histologic examination of a biopsy specimen taken from the right frontal bone showed a remarkable similarity.

OTHER BENIGN LESIONS

Other benign lesions of the skull may give a positive scan (Table 1). A 15 year old male with biopsy proven histiocytosis X had a past history of multiple lesions involving the skull, long bones, and spine dating back to the age of 7 years. A localized lytic lesion was found in the left parietal bone (Fig. 3*A*). The lesion was fairly typical for an eosinophilic granuloma, showing the margins to be bevelled and without sclerosis. A Tc^{99m} brain scan showed a definite area of increased activity in the location of the bone defect (Fig. 3, *B* and *C*).

Several patients with Paget's disease have had positive brain scans. Figure 4*A* is a typical example showing diffuse nodular sclerosis of the calvaria typical of osteitis deformans in a 70 year old female. The corresponding brain scan (Fig. 4*B*) showed increased activity near the vertex in the region of the sclerotic nodules.

A patient with a biopsy proven hemangioma of the calvaria also demonstrated a localized area of increased activity at the site of the lesion utilizing Tc^{99m}. Other authors have described positive scans in cases of hyperostosis frontalis interna, osteomyelitis of the skull, and scalp trauma.[4,6,10]

Positive scans due to craniotomy defects and burr holes are, of course, quite frequent but are usually regarded as being related to an inflammatory reaction in the underlying meninges and brain.

MALIGNANT LESIONS

Positive brain scans have also been recorded with malignant neoplasms involving the skull, both primary and secondary. Roentgenograms of the skull in a 12 year old male with seizures and hypertensive encephalopathy revealed a localized thickening of the calvaria with spiculation arising from the external margin in a manner most typical of metastatic neuroblastoma (Fig. 5, *A* and *B*). The brain scan showed a focus of increased activity in the posterior parietal region over the convexity of the brain on the left side in a location corresponding to a clinically palpable bone mass (Fig. 5, *C* and *D*). At craniotomy, a large vascular mass protruding both externally and internally from the parietal bone was exposed. The tumor was confined to the epidural space without gross or histologic evidence of invasion through the dura. Several similar cases have recently been described by Carter and associates.[2] Although craniectomy with excision of the localized mass produced an abatement in the patient's severe symptoms, diffuse skull metastases continued to progress.

Three patients with bone metastasis to the skull from carcinoma of the breast have had positive scans with the foci of increased activity corresponding to both lytic and blastic metastases. In this series of 14 cases, 1 patient had a primary malignancy of the calvaria, a fibrosarcoma.

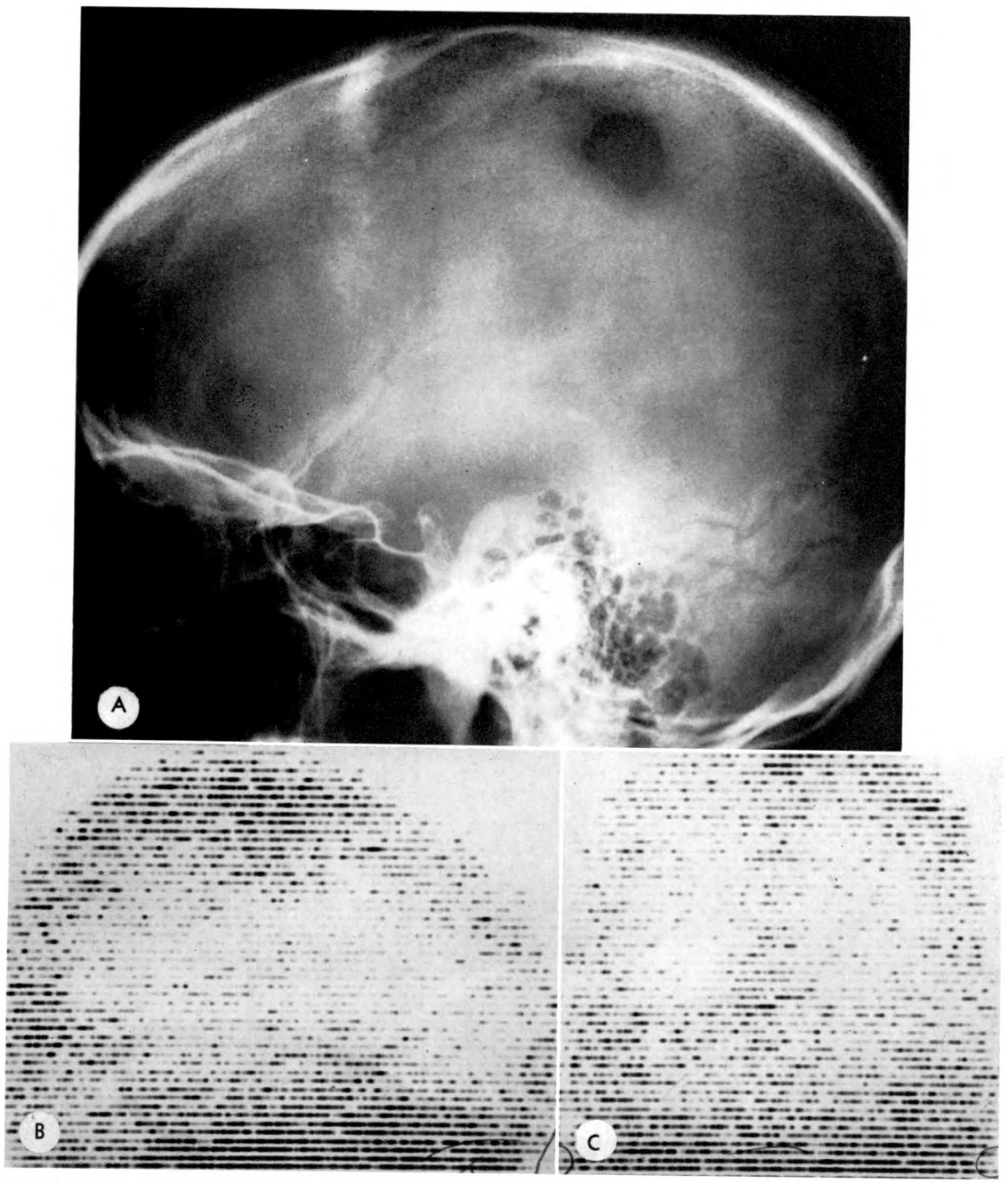


FIG. 3. Histiocytosis X in a 15 year old male. (*A*) Localized lytic lesion in left parietal bone with bevelled edges which are not sclerotic. (*B* and *C*) Tc^{99m} scans (10 mc). The peripheral focus of increased activity corresponds to the bone lesion.

DISCUSSION

All of the positive scans presented here were made with Tc^{99m}. Wagner[10] has classified this isotope as an "ionic extracellular substance" which equilibrates with the extracellular fluid space of a tumor. On the other hand, he defines I^{131} albumin and Hg^{197} chlormerodrin as "protein-bound substances," implying that the latter may actually be bound to the tumor cell or its

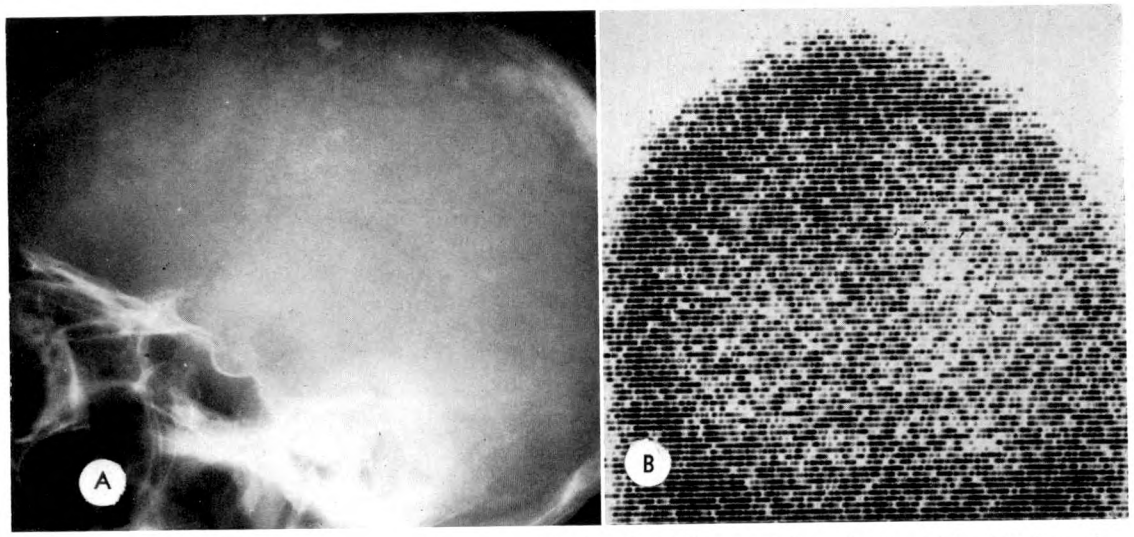


Fig. 4. (*A* and *B*) Paget's disease in a 70 year old female. Diffuse nodular sclerosis of the left frontal and parietal bones with zone of increased activity near vertex on Tc^{99m} scan (anterior view).

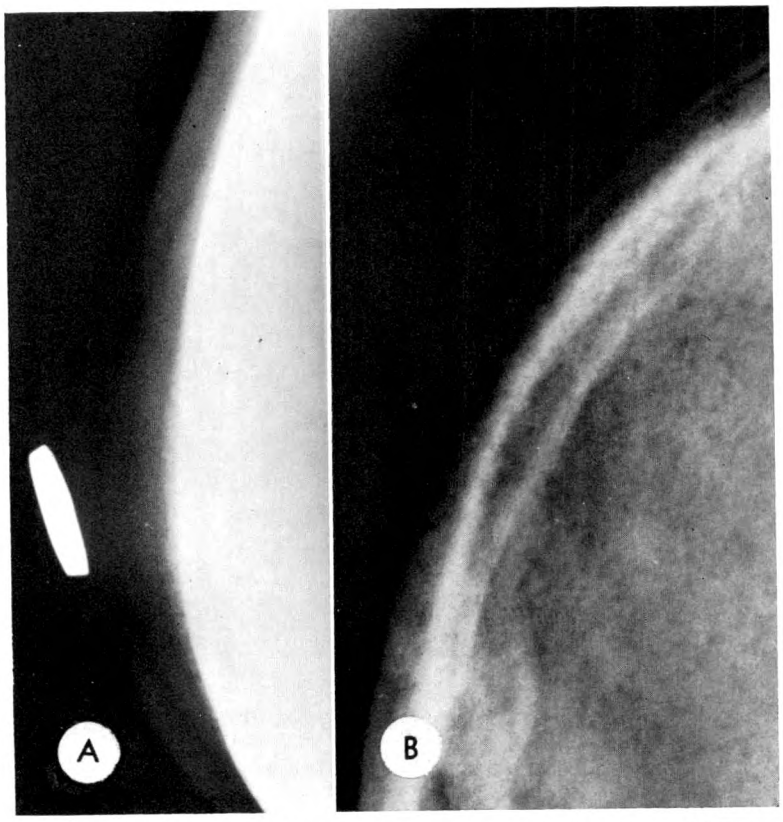


Fig. 5. Neuroblastoma metastatic to the calvarium in a 12 year old male. (*A* and *B*) Tangential views of the left parietal bone showing localized thickening of the calvarium and overlying soft tissue mass. Diffuse punctate radiolucencies within the thickened bone. Spiculated new bone arising from external margin.

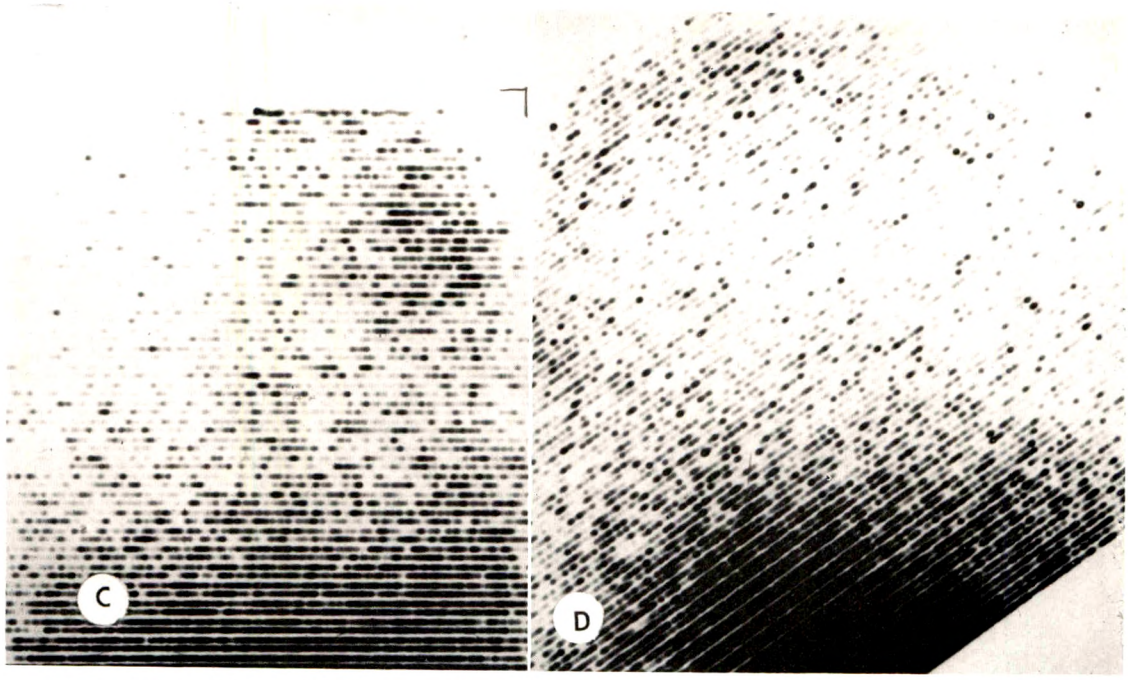


FIG. 5. (*C* and *D*) Tc^{99m} scans (10 mc). There is focal increased activity at the site of the bone lesion.

constituents. The common denominator of all the pathologic processes presented herein appears to be increased vascularity. Angiographic examinations in patients with fibrous dysplasia demonstrate enlarged ophthalmic and external carotid branches supplying the involved bone. It might therefore be postulated that Tc^{99m}, which normally gives a prominent vascular pattern on the brain scan, would be more apt to show a positive focus of activity in these lesions of the skull than the isotopes used earlier for brain scanning. This isotope has also been used to demonstrate lesions outside the region of the cranium, including carcinomas of the lung, pancreas, and rectum as well as malignant lymphomas and sarcomas of long bones.[1] Carcinomatous metastases to the long bones and spine may also yield positive scans with Tc^{99m}. When compared with studies using isotopes more specific for bone such as F^{18} or Sr^{87m}, the foci of activity are not as dense or as discrete,[7] but this evidence also suggests that the vascularity of a tumor or other pathologic process accounts for the Tc^{99m} uptake.

Roentgenographic differentiation of the sclerotic form of fibrous dysplasia involving the sphenoid and frontal bones from meningioma bone is difficult.[3] Meningioma *en plaque* involving the body or wings of the sphenoid bone is fairly common. Although the bone involved with fibrous dysplasia is usually more homogeneous and symmetric than meningioma bone, absolute differentiation is frequently impossible. It would appear that differentiation on the basis of a Tc^{99m} scan is also impossible. One might postulate, however, that a mercury scan would be less apt to give such a strongly positive uptake, and it is planned in the future to evaluate these patients with both scanning agents.

SUMMARY

Positive "brain" scans have been obtained in a number of benign and malignant lesions of the bony calvaria utilizing Tc^{99m} as the scanning agent. The vascu-

larity of these processes may account for the uptake of Tc^{99m}. It is important therefore to always closely correlate the roentgenographic examination of the skull with the brain scan.

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LIVER AND SPLEEN SCINTISCANNING WITH INDIUM 113m*

A CLINICAL PATHOLOGIC CORRELATION

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THE short-lived radionuclide indium 113m has broad application in nuclear medicine by virtue of its short physical half-life, long parent half-life, relatively low cost, and ease of chemical preparation of organ specific compounds.[2–5] Indium 113m colloids are now routinely used in our laboratory for liver and spleen scanning. Initially we prepared the radiocolloids by adjusting the pH of the eluent with sodium phosphate and adding gelatin as stabilizer.[1] More recently we have developed pre-prepared vials into which the generator is eluted directly to result in organ specific liver and spleen scanning agents. The ease with which organ specific compounds can be prepared, in addition to the wide range of organs which can be scanned with this radionuclide, *e.g.*, lung, brain, bone, bone marrow, blood pool, liver and spleen, foretells wide clinical application if its clinical efficacy can be established. The use of indium 113m for liver and spleen scans in 331 patients is presented.

METHODS AND RESULTS

Indium 113m eluted from a tin 113 generator* was used in 331 successive patients referred to the Nuclear Medicine Division of the Edward Mallinckrodt Institute of Radiology.

LIVER SCANS

The radiopharmaceutical was prepared as previously described[1] or eluted directly into pre-prepared vials containing sufficient sodium phosphate buffer (pH 7.5) to adjust the final mixture to pH 3.5. After intravenous injection of the isotope, scanning was performed on 1 of 2 rectilinear scanners† in addition to gamma camera imaging.‡

Two views of the liver (anterior and right lateral) were taken routinely. The scans were interpreted and the patients' charts were reviewed at follow-up. Thus far, we have obtained 196 clinical and pathologic follow-up studies which may be divided into 6 groups:

Group 1—Pathologically proven intra- and extrahepatic malignancies.
Group 2—Cirrhosis of the liver.
Group 3—Fatty liver.
Group 4—Hepatitis.
Group 5—Patients with positive scans and miscellaneous diseases.
Group 6—Normal.

In order to manifest objectivity in scan interpretation, the liver scans were independently classified as to size and homogeneity of activity: normal (Fig. 1); hepatomegaly (Fig. 7); uniformly diffuse poor function (Fig. 2); multiple small or large cold areas (Fig. 3 and 4); and single cold area (Fig. 5). Additional observations recorded independently were the appearance of activity in bone marrow and blood pool.

1. *Malignancy* (Table 1). Seventy-seven patients with histologically proven extrahepatic primary tumors were evaluated for possible hepatic metastases by indium

* Obtained from Neisler-Union Carbide, Tuxedo, New York.

† Nuclear Chicago Phodot and Picker Magna 5.

‡ Anger Camera, Nuclear Chicago, Co. (pho-gamma camera).

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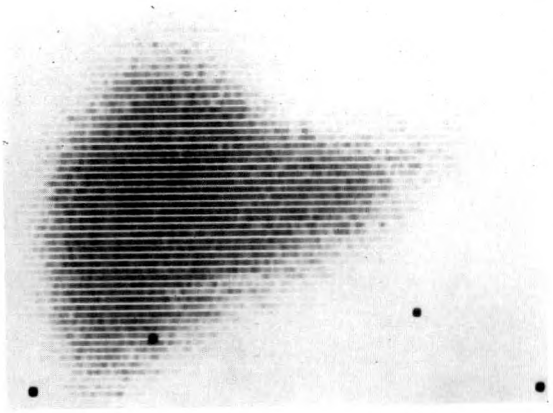


FIG. 1. Normal liver scan, anterior view.

113m liver scanning. Scanning was also performed in 2 patients with suspected hepatomas. The scans were positive in 50 and negative in 29 patients. Thirty-four of the patients with positive scans had liver tissue diagnoses by either needle biopsy, surgical biopsy and/or autopsy. In addition, 12 tissue diagnoses were obtained from 11 patients with known extrahepatic malignancy who had normal scans and histologically established normal livers. In this group there were 2 positive scans in patients with histologically normal livers and 1 negative scan in a patient with hepatic lesion (metastatic tumor) established by surgery. The 32 histologically confirmed positive liver scans revealed: hepatomegaly in 22 patients; multiple large cold areas in 16; multiple small cold areas in 6; a single large cold area in 3; and diffuse poor hepatic function in 5 patients. Splenomegaly was also observed in 6 patients.

A pattern of diffuse poor function in the scans was seen in histologically proven diffuse diseases of the liver; *e.g.*, leukemias. In addition, 1 patient with diffuse poor function had a histologically normal liver.

Of some significance in this study was a correlative assessment of other hepatic function studies in patients who were subsequently shown to have hepatic metastases. In 32 patients with positive scans, the alkaline phosphatase was abnormal in 25, SGOT in 17, total bilirubin in 17, and protein abnormalities were detected in 15.

2. *Cirrhosis of the liver.* Fifteen patients with cirrhosis of the liver were also studied. Diffuse poor function was observed in all 7 patients with tissue diagnoses. This was the most common pattern seen in cirrhosis. Other diagnostic features in the scans included enlarged spleen with increased spleen activity (5/7), hepatomegaly (3/7), prolonged blood pool activity (2/7), and increased bone marrow activity (3/7). Alkaline phosphatase was elevated in 4/7,



FIG. 2. Diffuse poor function, uneven distribution of activity in liver with splenomegaly. This patient had postnecrotic cirrhosis. Anterior view.

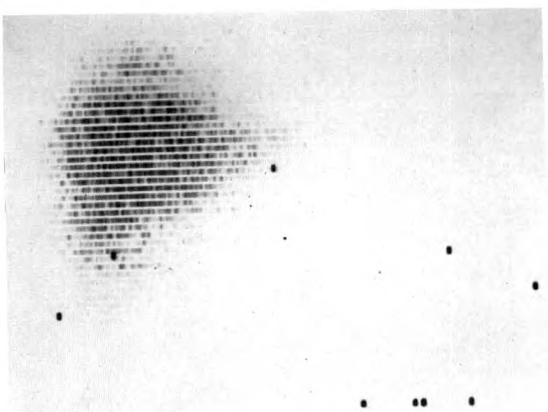


FIG. 3. Small liver with multiple small cold areas. This patient had carcinoma of the pancreas with multiple metastases to liver. Anterior view.

SGOT in 5/7, bilirubin in 4/7, BSP in 7/7, and protein abnormalities were seen in 3/7 of the patients.

3. *Fatty liver.* Eight patients who were subsequently shown to have fatty liver (tissue diagnosis) underwent liver scanning. Again, diffuse poor function and hepatomegaly were the most common scan patterns. Hepatomegaly was diagnosed in 7/8 and diffuse poor function in 6/8. Splenomegaly was observed in 3/8.

Liver function tests in this group of patients were less revealing than scans. Alkaline phosphatase was positive in 2/8 patients, SGOT in 2/8, BSP in 5/8, bilirubin in 1/8, and protein abnormalities were seen in 3/8.

4. *Hepatitis.* Nine patients with clinical hepatitis were referred for liver scanning. Scans were normal in 4 patients, and in the other 5 patients the following abnormalities were seen: diffuse poor function (5/9), hepatomegaly (5/9), and splenomegaly (2/9). Tissue diagnosis was established by needle biopsy in 6 and surgical biopsy in 3 of the patients.

In this group, liver function tests were more reliable in assessment of liver disease than scans. SGOT was the most commonly positive test (8/9), while BSP and alkaline phosphatase were equally positive (7/9). Only 6 of these patients were jaundiced.

5. *Patients with positive scans and miscellaneous disease.* In this group of patients,

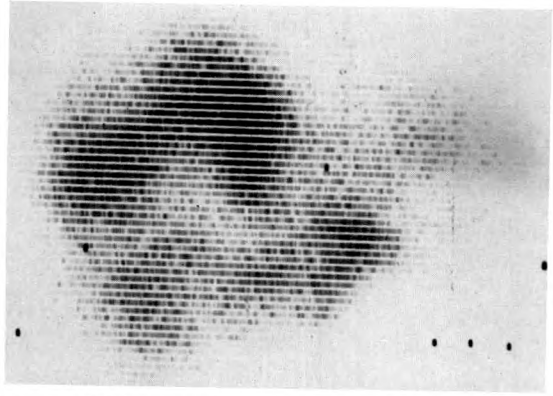


Fig. 4. Multiple large cold areas. Metastases from carcinoma of the colon. Anterior view.



Fig. 5. Solitary cold nodule. Metastasis from carcinoma of the colon. Anterior and right lateral view.

2 warrant discussion. Fever of undetermined origin was a clinical problem in 1 patient. The indium 113m liver scan showed a single large cold area. Surgery established the diagnosis of hepatic abscess. The second patient developed postoperative obstructive jaundice. A large cold area in the scan was observed, associated with elevated SGOT and alkaline phosphatase. This patient had ligation of a branch of the hepatic artery with resultant liver necrosis.

6. *Normal livers.* In 63 patients without known primary malignancies normal liver scans were obtained. Thirteen had tissue diagnosis (surgery 7, biopsy 4, autopsy 2) which revealed normal livers. The remaining 50 patients had no pathologic correlation.

SPLEEN SCANS

The spleen scanning agent was prepared as described previously[1] or by eluting the generator directly into pre-prepared vials containing sufficient sodium phosphate buffer (pH 7.5) to bring the pH of the final solution to pH 6. Following vigorous shaking and assay, 2–4 mc of this material was used for spleen scanning, with 3 views (anterior, posterior, left lateral) taken routinely. In assessing the spleen scans the size of the spleen was evaluated in the posterior view, and the splenic activity was graded as homogeneous poor function or discrete cold areas.

Thirteen patients were referred for spleen scanning for one of the following indica-

TABLE I

DATA FROM 32 PATIENTS WITH KNOWN MALIGNANCY AND ABNORMAL LIVER SCANS

Site or Type of Primary Malignancy	Age	Sex	Diagnosis Obtained by	Alkaline Phosphatase	SGOT	Protein Abnormality	Bilirubin	Objective Reading of the Scans
1. Colon	61	M	Surgery	+	−	−	−	Hepatomegaly. Single large cold area
2. Colon	70	F	Surgery	+	+	+	+	Hepatomegaly. Multiple large cold areas Increased spleen activity
3. Colon	53	M	Autopsy	+	+	+	+	Hepatomegaly. Multiple large cold areas
4. Colon	71	M	Biopsy	+	−	−	−	Hepatomegaly. Multiple large cold areas
5. Colon	72	F	Biopsy	+	+	−	+	Hepatomegaly. Single large cold area
6. Colon	36	F	Biopsy	+	+	−	+	Normal size liver. Multiple small cold areas
7. Colon	72	M	Surgery	−	+	+	−	Diffuse poor function. Splenomegaly
1. Carcinoid	40	F	Surgery	−	−	−	−	Multiple small cold areas
2. Carcinoid	47	F	Surgery	−	+	−	−	Hepatomegaly. Multiple large cold areas
1. Hepatoma	70	M	Biopsy	+	+	+	+	Hepatomegaly. Multiple large cold areas
2. Hepatoma	69	M	Biopsy Autopsy	+	+	+	+	Multiple small cold areas
1. Pancreas	56	M	Surgery	+	+	−	+	Hepatomegaly. Multiple small cold areas
2. Pancreas	62	M	Surgery	+	+	−	−	Hepatomegaly. Multiple large cold areas. Splenomegaly
3. Pancreas	72	F	Biopsy	+	+	+	+	Hepatomegaly. Multiple small cold areas
1. Stomach	50	F	Surgery Autopsy	+	−	+	+	Hepatomegaly
2. Stomach	75	M	Biopsy Autopsy	−	−	−	−	Hepatomegaly. Multiple large cold areas
1. Kidney	54	M	Surgery	+	−	−	−	Hepatomegaly. Single large cold area
1. Uterus	59	F	Biopsy	+	+	+	+	Hepatomegaly. Multiple large cold areas
2. Uterus	67	F	Surgery	+	−	−	−	Multiple small cold areas
1. Reticulum cell sarcoma	72	F	Biopsy	−	−	−	−	Hepatomegaly. Multiple large cold areas
1. Hodgkin's disease	44	F	Biopsy	+	+	+	+	Hepatomegaly. Multiple large cold areas
1. Acute monocytic leukemia	61	F	Autopsy Biopsy	−	−	+	+	Hepatomegaly. Diffuse poor function. Splenomegaly
2. Chronic lymphatic leukemia	39	M	Autopsy	−	−	−	+	Hepatomegaly. Diffuse poor function
3. Chronic lymphatic leukemia	32	M	Autopsy	+	+	+	+	Hepatomegaly. Diffuse poor function. Splenomegaly
1. Primary unknown	75	M	Biopsy	+	−	−	−	Multiple large cold areas
2. Primary unknown	68	M	Surgery	+	+	+	+	Multiple small cold areas
3. Primary unknown	70	M	Biopsy	+	−	−	−	Multiple large cold areas
4. Primary unknown	56	F	Biopsy	+	+	+	+	Hepatomegaly. Diffuse poor function. Splenomegaly
5. Primary unknown	15	M	Surgery	+	+	+	+	Hepatomegaly. Multiple large cold areas. Splenomegaly
6. Primary unknown	67	M	Surgery	+	−	+	−	Multiple large cold areas
7. Primary unknown	62	M	Biopsy	+	−	−	−	Multiple large cold areas
8. Primary unknown	79	M	Biopsy	+	−	−	−	Hepatomegaly. Multiple large cold areas
Totals	32			25	17	15	17	

tions: (a) Differential diagnosis of left upper quadrant masses; (b) evaluation of left upper quadrant pain; (c) evaluation of trauma to the left upper quadrant; (d) evaluation of spleen size and accessory spleens; (e) classification of Hodgkin's disease and lymphomas: (f) evaluation of splenic function; and (g) congenital heart disease.

Two patients are presented here as examples of the utility of this procedure.

CASE 1. A 43 year old white male was referred for spleen scanning for investigation of hyper-

bilirubinemia and a palpable spleen of undetermined etiology. The remaining physical and laboratory tests were within normal limits. The spleen scan (Fig. 6) revealed an inferiorly displaced normal sized spleen which appeared to have extrinsic impingement upon the superior pole. This 10 cm. clear area above the spleen was felt to be consistent with a post-traumatic cyst which was subsequently confirmed at surgery.

Case II. A 22 year old Negro male with known sickle cell disease was admitted complaining of severe left upper quadrant pain. Physical examination revealed hepatosplenomegaly and he was, therefore, referred for spleen scanning (Fig. 7) which demonstrated only a small area of isotopic accretion (3–4 cm.) located in what appeared to be the region of the inferior tip of the spleen on the abdominal roentgenogram. The remaining splenic tissue had no isotopic uptake, suggesting a large infarct in a nonfunctioning large spleen. The patient subsequently had confirmatory surgery. The only normal appearing splenic tissue found was at the lower tip of the spleen corresponding with the exact area of indium 113m uptake.

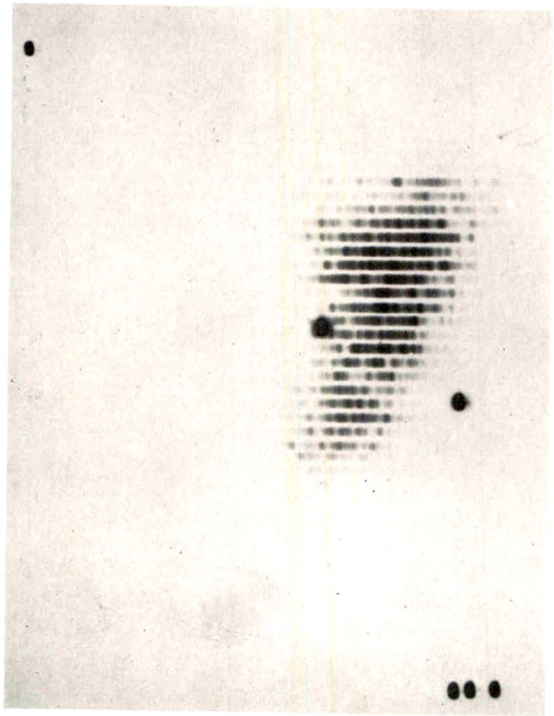


Fig. 6. Case I. Spleen normal in size, but displaced downward by a mass located in the left upper quadrant. Anterior view.



Fig. 7. Case II. Hepatomegaly, with uniform activity. Small area of functioning spleen tissue was located at the inferior border of the liver. Anterior view.

DISCUSSION

Indium 113m has been shown to be an easily prepared, reliable radiopharmaceutical for identification and evaluation of the regional function of the liver and spleen. Our observations in 45 patients with primary neoplasia demonstrate that indium 113m can be as effective for liver scanning as previously available radionuclides. When comparing our data with previous studies on technetium 99m hepatic scans, there is no significant difference in the clinical merits, despite the fact that the lower energy technetium may be better for purposes of anatomic resolution.

Thus, the hepatic uptake of indium 113m radiocolloid is equivalent to other forms of phagocytic hepatic scans and offers the advantages of a broad spectrum scanning agent which can be used for many other organ systems. These observations are consistent with previous colloid clearance studies which reveal increased blood pool, bone marrow, and splenic activity (*i.e.*, diminished hepatic colloid clearance) as evidence of chronic disease (*e.g.*, cirrhosis) rather than malignancy. The recognition of this pattern may be helpful in interpreting liver scans; however, with indium com-

plexes only a slight change in the final pH can result in increased splenic uptake of the radiocolloid without hepatic disease.

The suggestion has been made that splenic uptake is a combination of 2 factors: (1) reticuloendothelial clearance and (2) splenic clearance of materials similar in size to senescent red cells.[6] This concept is consistent with our observations of the splenic visualization obtained with indium 113m radiocolloid which appears to be in part due to splenic reticuloendothelial function. Increased splenic uptake of liver colloid is seen in hepatic insufficiency, and an increase in the final pH from pH 3.5 (liver) to pH 6 (spleen) results in a threefold increase in splenic uptake. This apparently is due to an increase in particle size.

The previously recommended radiopharmaceuticals for splenic scanning include chromium 51 labeled heat treated red blood cells, which depend upon early splenic sequestration of damaged cells. The preparatory technique is difficult and requires careful attention to incubation time and temperature for splenic visualization. The cells must be sufficiently treated to become spherical, but not excessively treated or hemolysis may result. This method was improved upon by the advent of brom-mercuro-hydroxy-propane (BMHP) labeled with either mercury 197 or mercury 203.[8] This radiopharmaceutical labels the cells and sufficiently damages them to produce immediate splenic sequestration. Unfortunately, BMHP is not commercially prepared, and thus, not widely available.

The ease of preparing organ specific compounds for brain, liver, lung, cardiac pool, bone and bone marrow scanning suggests that it may become a most useful agent for splenic scanning.

SUMMARY

Three hundred and thirty-one consecutive patients had liver and spleen scanning performed with indium 113m. A pathologically correlated follow-up was obtained in 92 instances.

The specific patterns recognized on the indium 113m liver scan were correlated with the disease entity, suggesting that the indium 113m agent is at least equivalent to previously available radionuclides for hepatic reticuloendothelial demonstration.

In addition, minimal changes in preparatory techniques cause increased splenic accretion, affording a new and useful agent for routine spleen scanning.

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PREPARATION AND TESTING OF A STERILE Sn^{113}—In^{113m} GENERATOR*

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THE wide variety of readily available nuclides provides, to the Nuclear Medicine scientist, a great freedom of choice and requires that careful thought be given to selecting the one with optimum physical characteristics.[13] The user should not be content with what may already be available, but should consider the ideal radioisotope and chemical form for his purpose.[7]

The convenience of using nuclides in the forms that are commercially available is great. It avoids the problems of "milking" radionuclide generators and the chemical preparation of the radiopharmaceutical in a sterile, pyrogen-free form. The necessity of eluting and the sterile chemical preparation of compounds for injection are probably the greatest disadvantages of radionuclide generators, but the advantages of short-lived radioisotopes have made the use of these systems very popular.

Radioisotope generators make available short-lived radioisotopes thousands of miles from the site of production and provide a continuous source of short-lived radionuclides in the Radioisotope Laboratory. The first system of this type was developed in 1926 by Gioachino Failla[4] who obtained radon from its parent radium. Failla also coined, at that time, the term "cow" for the generator and "milking" for the elution operation. Since Failla's development, which was the only practical generator until the late 1940s when Winsche *et al.*[14] developed the Te^{132}-I^{132} system, more than 100 theoretically possible generators have been listed. About 20 of these can be considered practical and a small group of 6 are presently in clinical use.

Special attention has been given to one of these systems, Mo^{99}-Tc^{99m}, which is in most frequent clinical use at the present time. However, since the first Sn^{113}-In^{113m} generator was developed by Gillette,[6] and has subsequently become generally available, it has also attracted considerable interest in medical applications for the visualization of internal organs by scintillation scanners and gamma cameras.[5,8,9]

In^{113m} is a cation and can, therefore, be used for labeling compounds where anionic Tc^{99m} cannot be used. For example, indium forms stable chelates with a large variety of organic and mineral radicals such as EDTA and DTPA.[11] The only soluble mineral salts of indium are the halogens, sulfates, nitrates, and perchlorates, while a few others (such as ferrocyanides and iodates) are slightly soluble. Most of the other indium salts (phosphates, carbonates, etc.) and hydroxides, are extremely insoluble in water.

The preparation of short-lived radiopharmaceuticals in the clinical laboratory has a special problem: sterilization. Autoclaving is very reliable, but it may cause decomposition of a heat-labile product and it is also time-consuming in the case of short-lived materials. Most of the techniques presently in use to prepare radiopharmaceuticals labeled with In^{113m} depend upon terminal autoclaving to produce sterile compounds. In this paper practical methods of production and testing of sterile pyrogen-free eluent for clinical use from a sterile, closed system Sn^{113}-In^{113m} generator are presented.

PREPARATION OF THE GENERATOR

Our sterile system consists of 3 principal parts: the generator itself, the container for sterile eluent and an automatic syringe for delivering the desired amount of eluent to the generator. The first part was prepared

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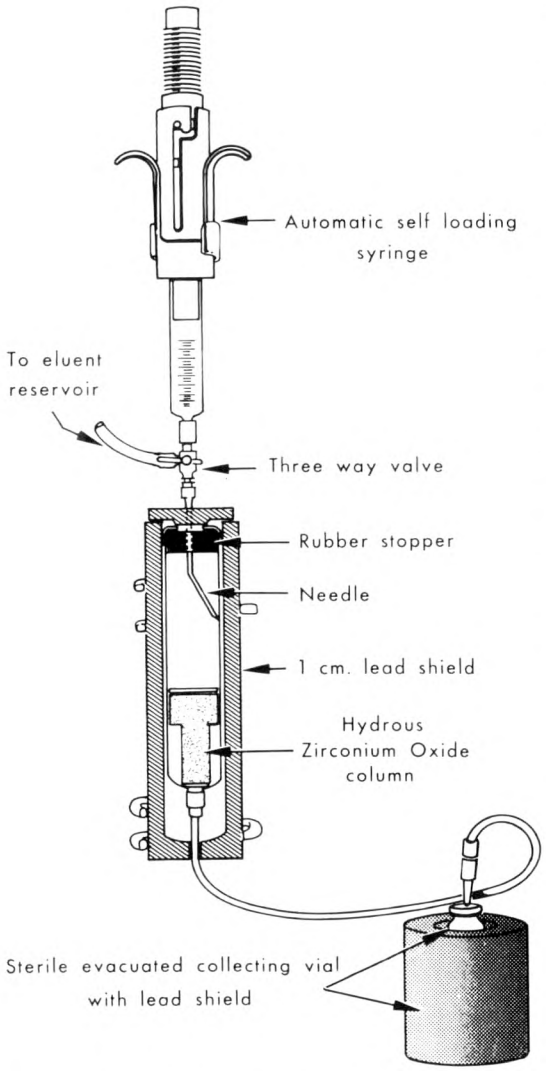


FIG. 1. Diagram showing the components of our sterile-closed system.

with a commercially available generator whose column consists of hydrous zirconium oxide[10] and was kept in a cylindrical lead shield, having a wall 1 cm. thick. To the top of this generator, an automatic syringe was permanently attached with a needle, which enters into the generator through a small hole drilled in the lead cap. This needle penetrates a rubber stopper attached to the top of the column. The needle has been bent slightly and does not point straight down the center of the column in order not to disturb the column during milking. A large (4 liter) Erlenmeyer flask containing eluent (HCl 0.05 M) is positioned above the generator and connected to the automatic syringe through a three-way valve, which operates in a manner that will let the syringe be charged with the eluent or will let the eluent be discharged from the syringe to the generator (Fig. 1). In this way leakage was prevented from the eluent container to the generator. The eluent container is airtight except for a curved, U form breather tube, partially filled with eluent solution, which has a cotton stopper in order to maintain sterility. A delivery tube with a disposable needle is connected to the bottom of the generator. The chromatographic column and the components were autoclaved and positioned as is shown in Figure 2. The preparation of this system for milking is very simple: operating the three-way valve in the proper manner, it is possible to fill the syringe with the desired amount of eluent. The syringe, filled with eluent solution, is depressed. After waiting 1 minute, the delivery tube is connected, using a new sterile needle each time, to an evacuated sterile vial, allowing

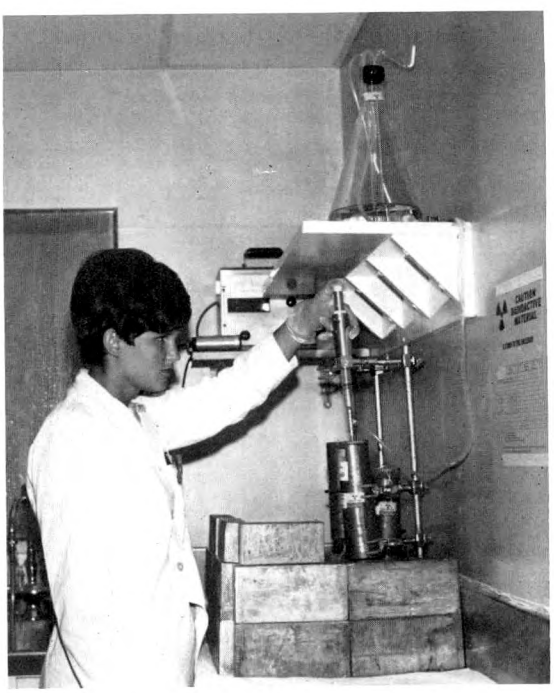


FIG. 2. Operation of elution of the generator.

the eluent to come out of the generator. When eluent ceases to be drawn into the evacuated vial, the milking is complete. The needle is removed from the vial and the three-way valve allows the automatic syringe to be refilled with eluent solution. Total time of milking is approximately 2 minutes.

TESTING THE GENERATOR

In order to be certain that the eluent can be safely used, it is not only necessary to test the generator for breakthrough of Sn^{113} and chemical impurities,[2] but to test for sterility and pyrogenicity as well. Our testing operations include the following:

RADIONUCLIDE PURITY

This is defined as the fraction of the total activity that is present in the form of the desired radionuclide. It is necessary to detect and measure the activity due to the parent breakthrough or any other nuclide present in the column, which is of great importance in relation to the radiation dose given to the patient, especially when parent or radioactive impurities are long-lived or β-emitting nuclides. These impurities are usually measured using one of the following techniques:

(a) *Physical methods.* These are retrospective procedures which are very useful in the examination of breakthrough of the parent when the half-life of the daughter is short, as is the case with the Sn^{113}-In^{113m} generator. The short-lived daughter is allowed to decay out and the presence of the parent, or any other long-lived radioactive impurity is then detected. In general this is performed by diluting and counting the eluent in a gamma well counter to determine the activity present at the time of milking. The same sample is recounted 24 to 48 hours later to determine the activity after all the In^{113m} present at the time of milking has decayed. A simple ratio of the 2 counts rate correcting for the original dilution factor is a measure of the gamma-emitting contaminants present. The Sn^{113} peak (255 kev.) is too close to the In^{113m} peak (393 kev.) to perform gamma spectrometry on the fresh eluent.

(b) *Chemical methods.* The presence of Sn nuclides can be detected in the eluent by spot colorimetric tests. Hematoxylin is useful for detection of minute amounts of tin (in the 0.1 μg. range) in the generator eluent immediately following elution.

CHEMICAL PURITY

The eluent can be impurified by other nonradioactive materials used as carrier or from constituents of the column itself. Our generator is packed with hydrous ZrO which is slightly soluble when the pH of the eluent solution is below 1.1.

For the chemical analysis of the eluent, emission spectrography, polarography, and colorimetric spot tests are particularly valuable.[2] Emission spectrography should be the method of choice, since it requires only a small sample and offers the opportunity of recording the presence of unexpected impurities. When a spectrograph is not available, spot tests are recommended.[5]

STERILITY AND APYROGENICITY

Levels of radioactivity and rate of decay for In^{113m} make these tests impossible prior to injection; thus, for sterility and apyrogenicity we must rely on careful operation and retrospective testing. Sterility tests were done three times a week and apyrogenicity tests once a month using the U.S.P. techniques.[12]

EFFICIENCY

The efficiency of the generator prepared as described, was tested after every elution in an ionization chamber. The ionization chamber was calibrated with a known Sn^{113}-In^{113m} standard source which was in equilibrium. The procedures for testing efficiency have been described elsewhere.[1]

RESULTS

This generator has been tested in our laboratory and used to produce sterile radiopharmaceuticals for over 4 months. The testing included checking three times weekly for sterility and once monthly for apyrogenicity. Breakthrough of Sn^{113} and other radionuclides as well as tests for chem-

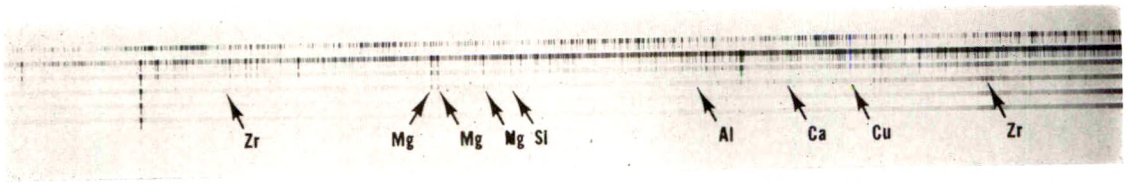


FIG. 3. Spectrogram obtained with eluate from generator, showing inert impurities present.

TABLE I

TESTING OF GENERATOR

Tests	Frequency of Tests	Number of Tests	Positive Results	Negative Results
Sterility	3 weekly	46	0	46
Apyrogenicity	1 monthly	4	0	4
Sn^{131} breakthrough	1 weekly	12	<0.002%	
Significant inert impurities	—	2	None	

ical impurities were carried out monthly.

The generator functioned normally during this testing period of 4 months. Radionuclide purity was well within acceptable limits (<0.02 per cent of Sn^{113}) and as is shown in the spectrogram of the eluate of the generator (Fig. 3), the inert impurities were very low. The amount of other metals present were in these ranges: Zr 2.5 μg./ml., Al 0.2 μg./ml., Ca 3 μg./ml., Cu 0.1 μg./ml., Mg 0.5 μg./ml., and Si 2.5 μg./ml. Sterility and apyrogenicity were never broken. Not a single growth of bacteria was observed during the testing period (Table 1). Pyrogen tests were always negative, and no patient reactions were observed in over 100 studies performed with this generator.

It is reassuring that, after many years' history of growing use, radiopharmaceuticals have had a remarkably good record for medical safety. We believe that the same safety can be maintained producing radiopharmaceuticals with sterile generator systems in the Laboratory of a Nuclear Medicine Department.

CONCLUSION

A Sn^{113}-In^{113m} generator, to produce sterile, pyrogen-free eluate, is described. The simplicity of preparation and operation of this generator providing sterile eluate is a great advantage in medical applications.

This generator was tested and found sterile and pyrogen-free over a 4 month period, during which time it was in daily use for patient studies.

The breakthrough of long-lived nuclides and contamination of the eluent with other chemicals was determined and found well within acceptable ranges for human use.

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LIVER IRRADIATION IN CHILDREN: ACUTE CHANGES WITH TRANSIENT LEUKOPENIA AND THROMBOCYTOPENIA*

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RECENTLY, we have reported 5 patients who have had irradiation to the intact liver and who have shown defects on radioisotope liver scanning within the irradiated volume. Each patient had been well clinically and had no laboratory signs of liver dysfunction. Biopsy revealed an unusual and distinctive histologic pattern in both the acute and chronic phases.[5]

This report describes 4 additional patients who have been observed recently and who did exhibit some degree of laboratory abnormality which we believe may be related to the acute effect of irradiation on liver. In each patient, a transient but marked depression of the peripheral platelet and white blood cell counts occurred at a time when the liver scan revealed a sudden acute defect within the irradiated area, a reversal of the ratio of radioisotopic concentration in spleen as compared to liver,[29] and abnormality by liver function tests.

Two patients underwent partial hepatic resection for hepatoma. Irradiation and chemotherapy, withheld until liver regeneration had occurred[8,9] as noted by follow-up scanning, were then begun. During this period of therapy, each patient developed acute diminished concentration of radioisotope within the irradiated liver, increased concentration in an enlarged spleen, abnormality of liver function tests and depression of both the peripheral white blood cell and platelet counts; the latter was relatively more marked than the former. One of these patients had a Cr^{51} platelet survival test that revealed diminished platelet survival and sequestration of platelets in the spleen; bone marrow examination was normal. Both patients showed reversal of all abnormal findings shortly after cessation of therapy.

Two additional patients showed a similar clinical pattern during the time when they were receiving chemotherapy and irradiation to the intact liver. The abnormal findings were temporary in each and reverted towards normal shortly after therapy was discontinued. Each patient was studied by selective arteriography which revealed changes due to the acute and late effects of radiation therapy.[17] Biopsy of liver of both patients, several months later, confirmed chronic radiation effect.[5,11,13,21]

REPORT OF CASES

I. Irradiation following partial hepatic resection.

Case 1. F.W., a 7 year old boy was well until October, 1967, when he developed diminished appetite at 3 weeks prior to admission to The Children's Hospital Medical Center (CHMC). Nausea without abdominal pain occurred shortly thereafter.

On admission, his abdomen was distended slightly. A firm, non-tender mass, 10 cm. below the right costal margin, appeared to be contiguous with the liver. The spleen was not enlarged. An Au^{198} colloid liver scan revealed irregularity to distribution of the radioisotope in the right lobe of the liver (Fig. 1). Hepatic arteriography revealed a large mass which was consistent with an intrahepatic malignancy.[17]

Laparotomy resulted in a right hepatic lobectomy to remove a lesion which was sub-

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sequently classified as a juvenile hepatoma. No gross involvement of the left lobe was observed.

Repeat liver scanning within 3 weeks of hepatic resection revealed symmetric distribution of isotope in the remaining liver tissue (Fig. 2). Liver function tests at this time were normal (Table I—Day 22).

He received no irradiation or chemotherapy and he remained well until February, 1968, when he developed symptoms of lethargy, diminished appetite and weight loss. An epigastric mass was palpable now; this was hard and slightly nodular. No enlargement of the spleen was detected. A repeat radioisotope scan of the liver revealed a deformity of the remaining liver tissue, probably due to recurrent tumor (Fig. 3). This was confirmed by hepatic arteriography.[17] A skeletal survey, including roentgenograms of the chest, showed no metastases.

At a second laparotomy, the central portion of the liver was intact; this conformed to the most medial portion of the left lobe and to the caudate lobe; a very large recurrent tumor was present within the left hepatic lobe, and 3 tumor nodules were present in the omentum. Excision of the large mass was accomplished but no gross tumor remained at the excision margin within the liver and in the omentum.

In order to allow liver regeneration to proceed unhindered, no therapy was instituted for

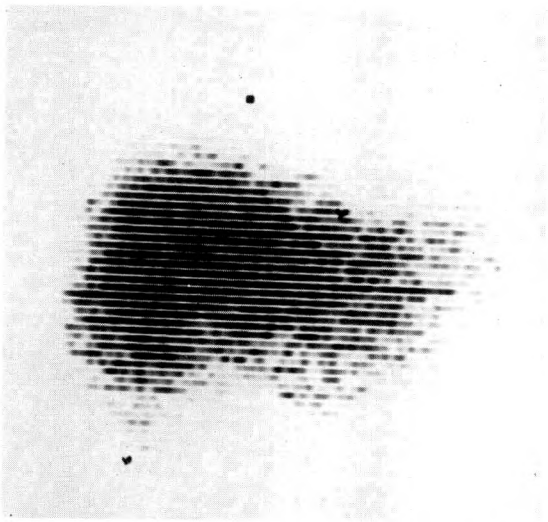


FIG. 1. Case 1. Au^{198} colloid scan of the liver (Day 0). There is irregular distribution to activity of radioisotope in the inferior portion of the right hepatic lobe. The distribution of radioisotope in the left lobe is normal. A juvenile hepatoma was confined to the right lobe.

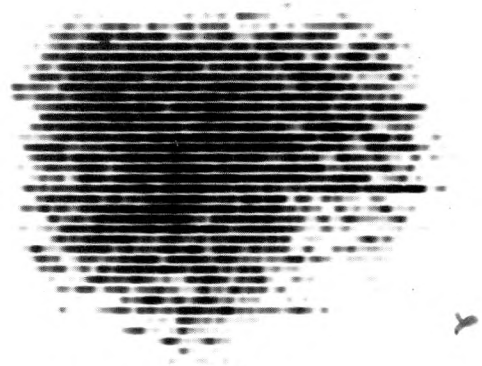


FIG. 2. Case 1. Au^{198} colloid scan of the liver (Day 22). There is uniform distribution of isotope at 3 weeks following resection of right hepatic lobe. Regeneration of liver volume is noted.

1 month following surgery.[7] At the end of this period, a repeat liver scan revealed satisfactory volume of the normal functioning liver to be present (Fig. 4, *A* and *B*). Peripheral blood cell counts (Fig. 5) and liver functions (Table I—Day 143) were still normal at this time.

Towards the end of March, 1968, irradiation was delivered to the abdomen to include all remaining liver tissue and the omentum. Radiation therapy consisting of 2,100 rads (250 kvp., 15 ma., 0.4 mm. Sn, 0.25 mm. Cu, 1.0 mm. Al added filter, half-value layer of 2.7 mm. Cu)* was delivered in 15 elapsed days through opposed anterior and posterior portals for the initial 1,200 rads, and then through lateral opposed portals in an attempt to spare underlying kidneys.[28] During this course of irradiation 5-fluorouracil (15 mg./kg. body weight)† was administered intravenously on 2 separate occasions (Fig. 5).

He remained well until early April, 1968, when his peripheral white blood cell and platelet counts became depressed suddenly. The platelet counts fell to as low as 15,500 and the white blood cell counts to 3,000 (Fig. 5, Day 157). Liver scanning at this time revealed diminished radioisotopic activity in the liver and

* All patients in this report were treated with the same factors.

† In all patients, chemotherapy was administered under the direction of Sidney Farber, M.D.

TABLE I

LIVER FUNCTION TESTS

CASE 1

Day	SGOT	Bilirubin (direct/total)	Alkaline Phosphatase	LDH	Remarks
22	30	0.2/0.3	10.8	125	3 weeks post partial hepatic resection
143	75	0.3/1.7	14.2	135	Prior to start of irradiation and 5-fluorouracil
164	725		9.4	235	Completion of irradiation and 5-fluorouracil. Abnormal scan and depressed peripheral cell counts. No further treatment delivered after this
185	126	1.35/2.1		390	
192	130	1.6/2.1		490	
199	198	1.8/2.1	15.2	200	
206	60	0.1/0.2	11.1	155	Normal liver scan. Normal peripheral blood cell counts
Day 0: Day of first admission for primary neoplasm	Normal: 10–40 units	Normal: 0.4/1.9	Normal: 5–15 Bodansky units	Normal: 42–98 units	

SGOT = serum glutamic oxalacetic transaminase. LDH = Lactate dehydrogenase.



an increased uptake by the spleen, a reversal of normal (Fig. 6). Shortly thereafter, his liver functions became abnormal (Table I—Day 165).

All therapy was discontinued and his peripheral counts reverted to normal. Liver scan reverted to a normal distribution ratio of liver to spleen and the diminished uptake within the liver was not apparent (Fig. 7).

In late July, 1968 (Day 255), the liver scan

FIG. 3. Case 1. Au^{198} colloid scan of the liver (Day 105). Deformity of liver configuration is present. There is a concavity along the lateral border and ill-defined inhomogeneous uptake of isotope in the medial aspect of the liver tissue. Recurrence was present in the lateral aspect of the liver. Arrow demarcates the xyphoid.

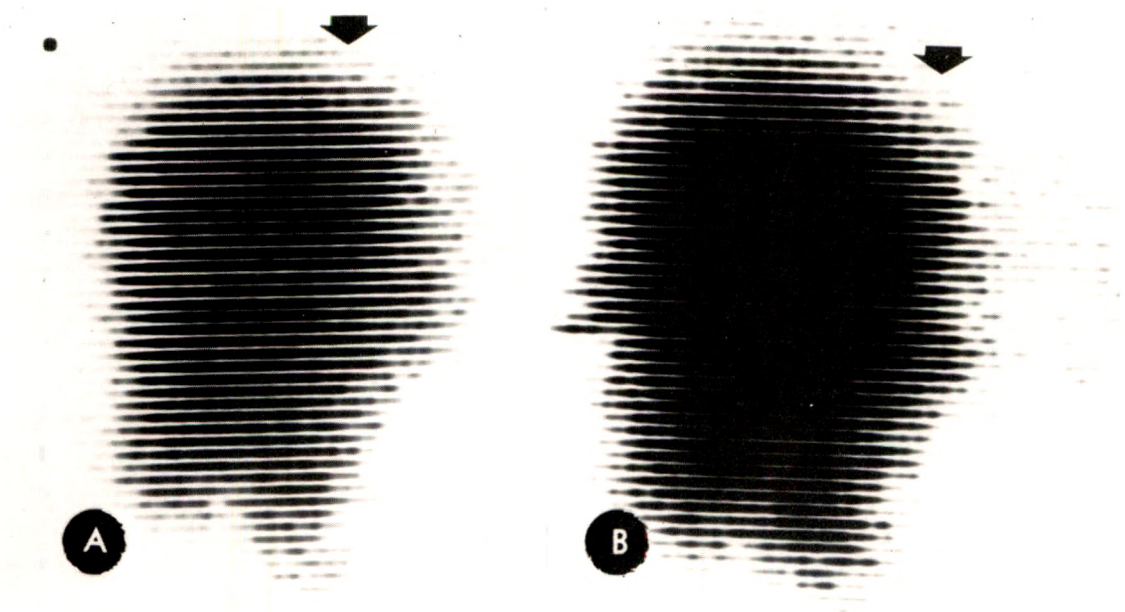


Fig. 4. Case 1. (*A*) Au^{198} colloid scan of the liver (Day 120). Some inhomogeneity of isotope distribution in the liver is apparent; the liver volume is enlarged. Distribution of colloid in the spleen is increased over normal and indicates some degree of liver dysfunction. These changes may be due to postoperative edema. (*B*) Au^{198} colloid liver scan at 3 weeks following resection of recurrent tumor (Day 145). The distribution of isotope in liver is homogeneous. The liver size is smaller and more normal; concentration of radiocolloid in the spleen has diminished. This improvement was interpreted as due to diminished postoperative edema and regeneration of liver tissue with resulting return of liver function to normal.

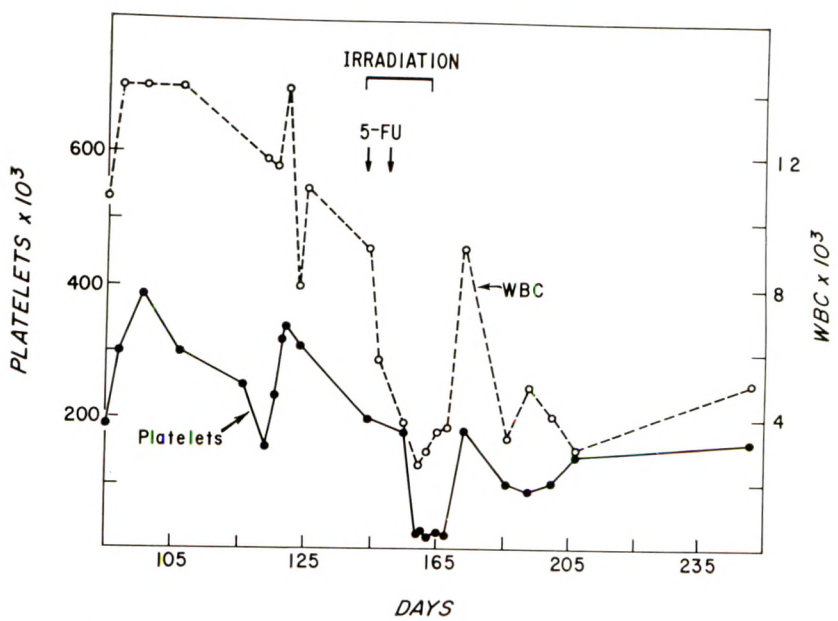


Fig. 5. Case 1. Graph relates the peripheral white blood cell count and platelet count to therapy. Day 105 is day of second admission for recurrent neoplasm.



FIG. 6. Case I. Au^{198} colloid liver scan (Day 165). There is diminished uptake of radiocolloid by liver and increased uptake in an enlarged spleen. These abnormalities occurred following irradiation and chemotherapy and were consistent with liver dysfunction.

remained unchanged with normal distribution of isotope in the liver as compared to spleen, and both his peripheral counts and liver function tests were not remarkable.

CASE II. K.O., a 5 month old girl, was found to have a large abdominal mass at routine physical examination. The mass filled the right abdomen and extended to the iliac crest; it was firm, non-tender and nodular.

A radioisotope liver scan revealed a defect to the homogeneous distribution of isotope in the liver (Fig. 8). Selective hepatic arteriography revealed abnormal vasculature and stretching of vessels in a similar region of the liver.[17] A chest roentgenogram and skeletal survey were normal.

Liver function tests revealed a slightly elevated level of SGOT, but were otherwise not remarkable (Table II). Peripheral white blood cell and platelet counts were within normal limits (Fig. 9).

At laparotomy, a primary embryoma was found in the left lobe of the liver; the left hepatic lobe was resected in continuity with a small portion of the medial right hepatic lobe.

Liver function tests became elevated in the immediate postoperative period but soon reverted towards the normal (Table II). A repeat radioisotope liver scan revealed normal function of the remaining right hepatic lobe; some increased isotope uptake by the spleen indicated diminished liver function and was consistent with the abnormal liver function tests (Fig. 10).

A chest roentgenogram within a few days of surgery revealed lung metastases. Within $2\frac{1}{2}$



FIG. 7. Case I. Au^{198} colloid liver scan (Day 206). A normal distribution of radioisotope in the liver and a normal ratio of distribution of isotope between the liver and spleen is apparent now. This is consistent with recovery of liver dysfunction.

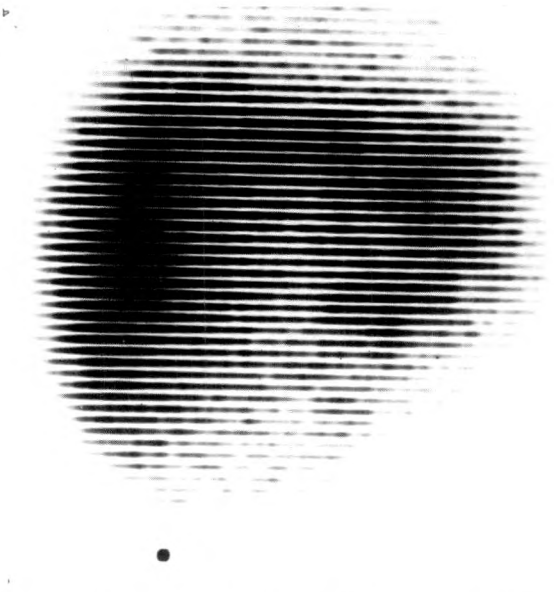


FIG. 8. Case II. Tc^{99m} sulfur colloid scan of the liver (Day 0). Diminished concentration of radiocolloid is noted in the central portion of the liver. An hepatic embryoma was present within the left lobe of the liver.

TABLE II

LIVER FUNCTION TESTS

CASE II

Day	SGOT	Bilirubin (direct/total)	Alkaline Phosphatase	LDH	Remarks
7	115	0.2/0.8	14.4		One week post partial hepatic resection
10	875	1.3/2.6	22.0	1650	Due to hepatic congestion ? ?
11	590		22.9	850	
13	145	1.1/1.7	19.3	480	
17	55	0.6/0.4	11.2	305	Irradiation and chemotherapy begun
41	55	0.6/0.6	4.6	235	Low peripheral cell counts noted. Period of abnormal scanning and diminished platelet survival
72	105	0.3/0.6	7.7	275	
74	590		22.9	850	Normal function by scanning. Peripheral cell counts normal
Day 0: Day of first admission for primary neoplasm	Normal: 10–40 units	Normal: 0.4/1.9	Normal: 5–15 Bodansky units	Normal: 42–98 units	

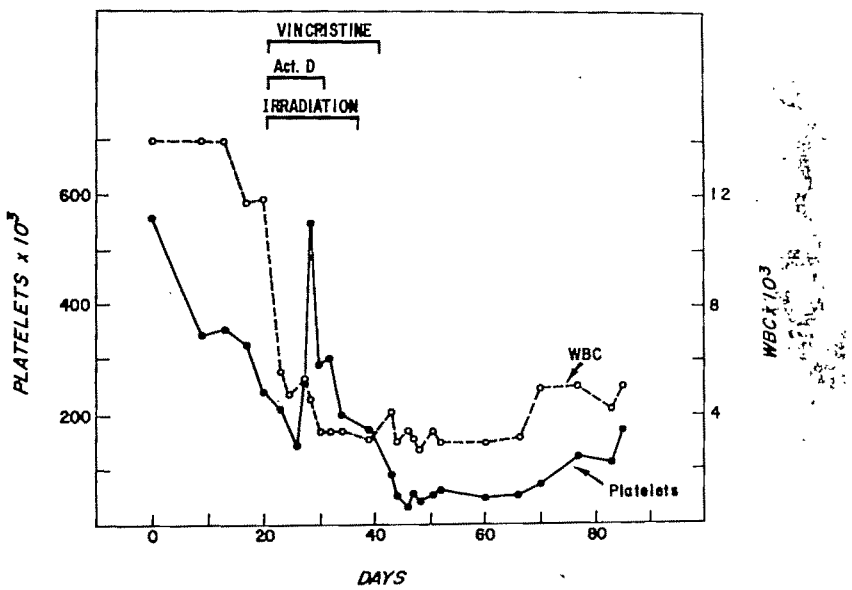


FIG. 9. Case II. Graph relates peripheral cell counts to therapy (see text). Day 0 is defined as day of first admission to Children's Hospital Medical Center.

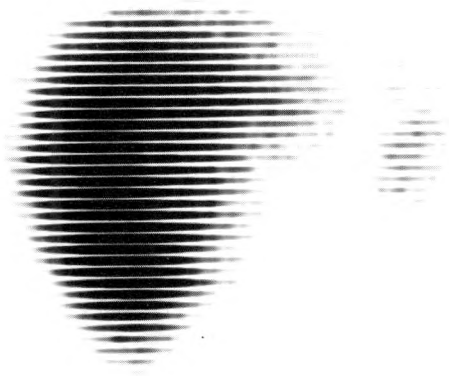


FIG. 10. Case II. Au^{198} colloid liver scan (Day 13). Following resection of the left hepatic lobe, there is fairly normal distribution of radioisotope in the right lobe; irregularity of distribution at medial surface may indicate postoperative effect from the procedure 2 weeks previously. Slight increased uptake in the spleen indicates minimal liver dysfunction.

weeks of partial hepatic resection, irradiation was delivered to the liver and to both lung fields. Radiation therapy consisting of 2,025 rads in 16 elapsed days was delivered to the former and 1,265 rads in 9 days to the latter. Chemotherapy, in the form of actinomycin D (70 μg./kg. body weight in 7 evenly divided doses, intravenously) and vincristine sulfate (0.05 mg./kg. body weight once per week, intravenously) was also administered during this period (Fig. 9).

At the completion of irradiation and chemotherapy the lung metastases disappeared.

Prior to the course of irradiation and chemotherapy, liver function tests tended more towards normal (Table II—Day 17); during this regimen, peripheral blood cell counts remained stable (Fig. 9). Suddenly, towards the completion of her therapeutic regimen, the peripheral platelet count became markedly depressed to levels of 30,000 to 40,000; her peripheral white blood cell count fell slightly but remained above 2,800. The liver function tests did not change.

A repeat radioisotope scan of the liver now showed diminished uptake in the liver and increased radioisotopic concentration of the colloid in the spleen (Fig. 11). A scan of the abdomen after the injection of Cr^{51} tagged to platelets revealed sequestration of platelets in the spleen (Fig. 12). This would correspond to diminished liver function and increased activity of the spleen.

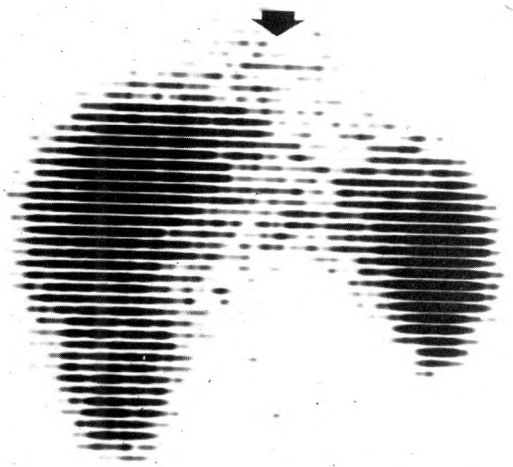


FIG. 11. Case II. Au^{198} colloid scan of liver (Day 52). The isotope has more irregular distribution than on previous examination. In addition, increased uptake in the spleen is noted. Irradiation and chemotherapy had been completed by this time.

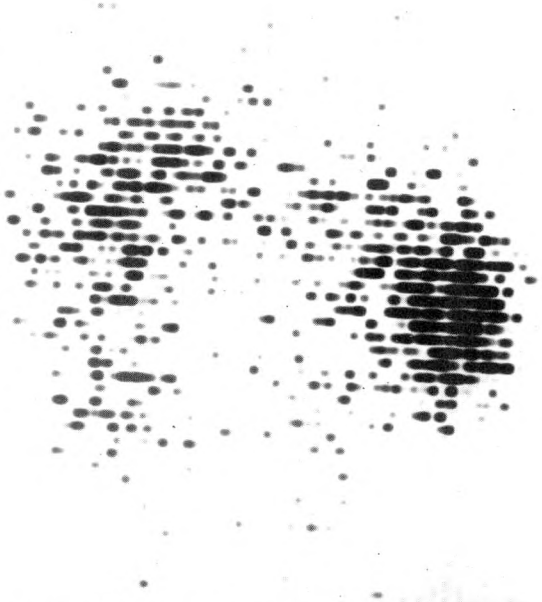


FIG. 12. Case II. Scan of the abdomen following injection of Cr^{51} tagged to platelets (Day 53) reveals sequestration in the spleen with minimal activity in the liver.

Platelet survival times revealed the half-life of platelets in this patient to be 1.2 days (normal: $3\frac{1}{2}$ days) and total platelet survival 3.1 days (normal: 8 days). Bone marrow at this time appeared normal; adequate numbers of megakaryocytes seemed to be present.

Over the following month, her peripheral counts rose to more normal levels (Fig. 9) and a repeat isotope liver scan showed a more normal distribution of the colloid between the liver and the spleen (Fig. 13). However, the liver function tests at this period became increasingly abnormal. During this time she developed recurrent lung metastases and superimposed pneumonitis, from which she died.

At postmortem examination, although her lungs revealed obvious tumor, no tumor was present in the liver. Instead, advanced changes of fibrosis and even hyaline deposition were present and conformed to one of the histologic patterns that we have reported previously as associated with irradiation.[5]

II. Irradiation to the intact liver.

Case III. A.C., a 6 year old boy, entered Children's Hospital Medical Center in July, 1967, because of painless hematuria and a right flank mass. The mass was firm and filled both the upper and lower quadrants of the right hemi-abdomen.



Fig. 13. Case II. Au^{198} colloid scan of the liver with Tc^{99m} pertechnetate-sulfide (Day 77). There is a normal distribution ratio between the liver and the spleen and uniform distribution of the compound within the liver.

Intravenous pyelography revealed a mass arising from the lower pole of the right kidney; a radioisotope scan suggested extrinsic pressure by the mass upon the liver.[4]

At laparotomy, the right Wilms' tumor was excised *in toto* in continuity with the right kidney; tumor was noted to have extended grossly into the inferior vena cava. One of 11 renal hilar lymph nodes was involved by tumor. A normal liver configuration was observed on a repeat liver scan in the immediate postoperative period.

In addition to the right renal fossa, radiation therapy was delivered also to both lung fields postoperatively as "prophylaxis"* because of possible embolization of tumor found in the inferior vena cava while the latter was manipulated at laparotomy. Radiation therapy consisting of 3,600 rads in 34 elapsed days was delivered to the right renal fossa, 1,135 rads in 8 days to both lung fields, and 2,335 rads in 24 days to the thoracic portion of the vena cava. Vincristine sulfate and actinomycin D were used intravenously (doses of each as described previously).

Within weeks he began to fatigue easily and he developed midline and supraumbilical abdominal pain. A localized defect in the uniform distribution of the radioisotope was noted by scanning (Fig. 14) and a tender 5×7 cm. abdominal mass was palpated in this area.

At a second laparotomy, a localized and discrete abscess was found in the right hepatic lobe. No tumor was obvious in the liver or right renal fossa. Following drainage of the abscess which cultured rare *Staphylococcus aureus*, he was discharged and received maintenance vincristine sulfate.

He remained well until mid-September, 1967, when he developed malaise, nausea and pain in the right upper quadrant and epigastrium. Physical examination now revealed a firm mass in the right upper quadrant, 4 fingerbreadth's below the costal margin and extending nearly to the midline. The vital signs were normal except for a temperature of 101°F. (oral).

Peripheral platelet and white blood cell counts were depressed suddenly to very low levels with possibly a more profound effect on

* "Prophylactic" irradiation of lung fields is not routine in this Center and is delivered only in most unusual circumstances.[27]



Fig. 14. Case III. Au^{198} colloid liver scan (Day 46). A defect in the normal distribution of isotope exists in the inferior portion of the right lobe of the liver. A localized abscess cavity was excised from this region.

the platelet count (Fig. 15—Day 66). The platelet count fell to the 10,000 level and the white blood cell count to the 1,600 level at one point. The liver function tests were somewhat abnormal now (Table III—Day 67). A bone marrow examination revealed hypoplasia of megakaryocyte formation.

Radioisotope liver scanning revealed a markedly diminished uptake of the colloid within the previously irradiated right lobe of the liver; increased uptake in the left lobe and/or spleen was evident (Fig. 16).

Selective hepatic arteriography revealed the liver to be enlarged. There was "sluggish" flow in the portal venous system and prolonged retention of contrast material in a slightly enlarged spleen. These findings were consistent with segmental or lobular hepatic vein obstruction[17,20] and therefore consistent with radiation effect upon the liver.[5,21]

All medication, including vincristine, was discontinued. He was discharged and evaluated carefully over the next few months. Within the first 3 weeks of observation, his peripheral white blood cell and platelet counts rose and were maintained at normal levels (Fig. 15), the liver enlargement regressed clinically, and a repeat liver scan showed improved distribution of the isotope (Fig. 17).

In late November, 1967 (Fig. 15—Day 118), a repeat course of actinomycin D was administered intravenously at half the original and standard dose. (Standard dose—10 μg./kg. body weight per dose for total of 70 μg./kg. body weight.) This was tolerated without obvious clinical effect or significant suppression of the peripheral counts.

Within 6 weeks, however, his liver function tests became grossly elevated, and he developed jaundice and general malaise (Table III—Day 180). A diagnosis of "infectious hepatitis" was entertained. His clinical condition improved and the liver function tests became normal in the ensuing 3 month period, or by the first part of April, 1968 (Table III—Day 263).

Some weeks later, in late April, 1968, a course of vincristine was started and continued

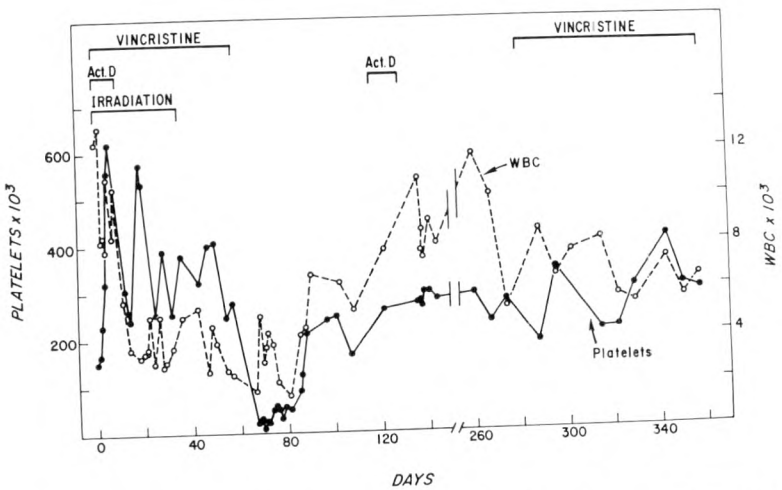


Fig. 15. Case III. Graph relates peripheral blood cell counts to therapy (see text).

TABLE III

LIVER FUNCTION TESTS

CASE III

Day	SGOT	Bilirubin (direct/total)	Alkaline Phosphatase	LDH	Remarks
67	90.5	0.2/0.2	10.5	230	Abnormal scan and depressed peripheral cell counts
81	110		16.0	155	
109	140	0.2/0.3	23.4	150	Scan improved. Peripheral cell counts normal
137	60		29.2	275	
180	1625	5.8/8.7	43	435	Clinical liver dysfunction ? ? "Hepatitis"
189	4000	14.8/19.8		750	
210		6.6/10.2			
217	220	4.4/7.3	12.1	130	
235	250	1.8/2.7	13.4	180	Clinical liver dysfunction improved
263	35	0.3/0.5	13.4	165	
Day 0: Day of first admission for primary neoplasm	Normal: 10–40 units	Normal: 0.4/1.9	Normal: 5–15 Bodansky units	Normal: 42–98 units	

through July, 1968 (0.05 mg./kg. each week). No adverse effects were noted. A liver scan in May, 1968, revealed further improvement in distribution of radiocolloid (Fig. 18).

In August, 1968, repeat selective arteriography revealed findings consistent with fibrosis of the right hepatic lobe and hypertrophy of the left.[17] This was consistent with the defect to radioisotope distribution now noted (Fig. 19). Biopsy of the liver revealed changes consistent with late radiation effect.[5,21]

CASE IV. L.G., a 4 year old girl, was admitted in late September, 1967, because of abdominal distention due to a hard mass which filled the entire right hemi-abdomen. The vital signs were normal but she appeared pale and cachectic.

Inferior vena cavagraphy revealed obstruction to the free flow of contrast material at the level of L_3. There was no visualization of contrast medium within the right kidney, which appeared to be enlarged; the left kidney functioned well and appeared to be normal. Roentgenograms of the chest disclosed multiple pulmonary nodules in both lung fields and a right pleural effusion.

Radioisotope liver scan revealed changes consistent with pressure by a mass posterior to the liver.[4]

A presumptive diagnosis of Wilms' tumor of the right kidney with pulmonary metastases was made. Because of her very poor general condition, surgical intervention at this time seemed unwise. Preoperative irradiation* and chemotherapy (actinomycin D—70 μg./kg.

* At this Center, preoperative irradiation is not routine for Wilms' tumor and is administered only in extraordinary circumstances.[27]

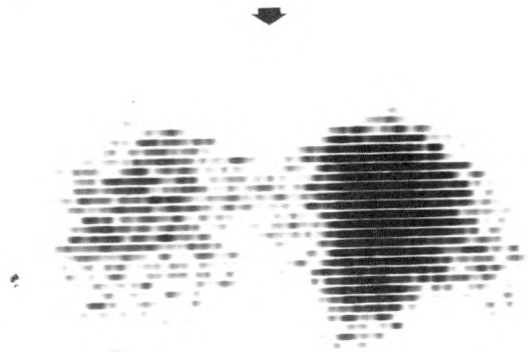


FIG. 16. Case III. Au^{198} colloid liver scan (Day 67). There is marked reduction to concentration of isotope in the irradiated right hepatic lobe. The increased uptake corresponds to the hypertrophied left lobe of the liver and/or spleen.

body weight in 7 equal daily doses; vincristine sulfate—0.05 mg./kg. body weight once per week) were begun. Radiation therapy consisting of 1,000 rads in 11 elapsed days was delivered to the right abdominal mass and 600 rads in 4 days to both lung fields.

At the end of this preliminary course of therapy, her abdominal mass regressed and the pulmonary lesions began to diminish. Peripheral white blood cell and platelet counts remained relatively stable.

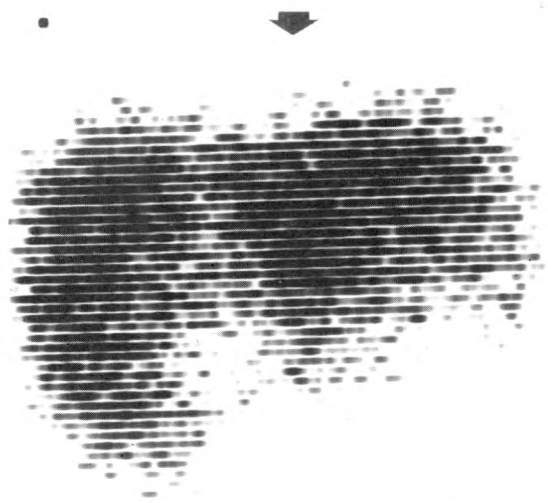


FIG. 17. Case III. Au^{198} colloid scan of liver (Day 111). The increased distribution of radioactivity in the area of previous defect is consistent with regeneration of liver tissue following irradiation.

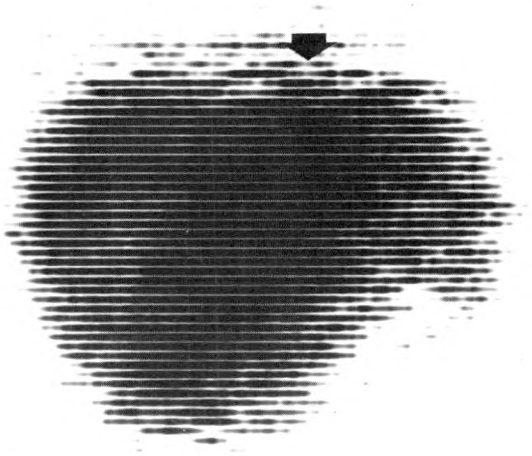


FIG. 18. Case III. Au^{198} colloid liver scan (Day 294) reveals further improvement in the liver concentration of the radioisotope.

In mid-October, 1967, she underwent laparotomy and a large Wilms' tumor was removed in continuity with the right kidney. Tumor filled the renal vein but did not extend into the inferior vena cava.

Postoperatively, additional irradiation was delivered. The total dose to the hemi-abdomen, including that delivered preoperatively, was 3,160 rads in 57 elapsed days and 1,260 rads in 23 days to both lung fields. Further chemotherapy was not instituted at this time.

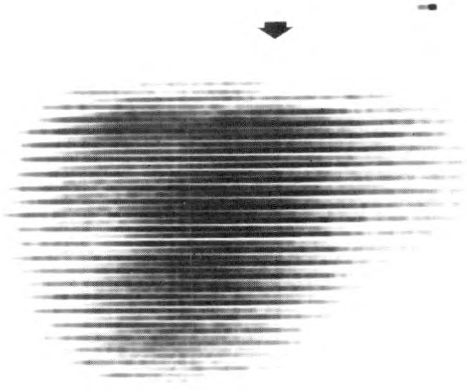


FIG. 19. Case III. Tc^{99m} sulfur colloid liver scan (Day 350). The defect in the right lobe of the liver is present at 1 year following irradiation. Arteriography revealed changes consistent with fibrosis of the right hepatic lobe and hypertrophy of the left lobe. Laparotomy confirmed this: a biopsy of the right hepatic lobe revealed changes consistent with late radiation effect.

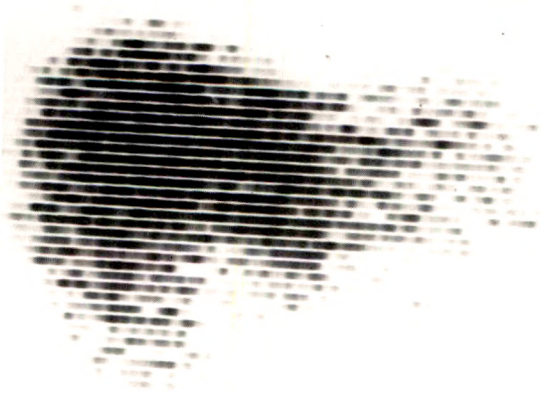


Fig. 20. Case IV. Au^{198} colloid liver scan (Day 30). There is irregular distribution of the isotope in the irradiated right hepatic lobe.



Fig. 22. Case IV. Au^{198} colloid liver scan (Day 290). A persistent defect of the right hepatic lobe is present. Laparotomy confirmed fibrosis of this area.

At the conclusion of this course of irradiation, a chest roentgenogram revealed complete resolution of all metastatic foci; a repeat inferior vena cavagram revealed a residual block at L3—this was interpreted now as due to fibrosis.

Radioisotope liver scanning revealed changes consistent with radiation effect (Fig. 20). At this time, her peripheral cell counts, which had been at normal levels, showed a suppression, more marked in the platelet count which fell to as low as 15,500, while the white blood cell count fell to a low point of 1,850 (Fig. 21—Day 46). With no definitive therapy, her white blood cell and platelet counts rose to normal levels within a short interval. Liver scanning now revealed an improved concentration of the isotope.

Within 6 weeks, a repeat course of actinomycin D (70 μg./kg. body weight as described above) was tolerated without significant peripheral cell count depression as was a third course after another 10 week interval (Fig. 21). Liver scanning at this time showed stability to configuration and isotope distribution (Fig. 22).

In late March, 1968, she was re-admitted for a second laparotomy to evaluate the inferior vena cava. Hepatic arteriography was consistent with the changes noted by liver scanning—the findings were consistent with fibrosis of

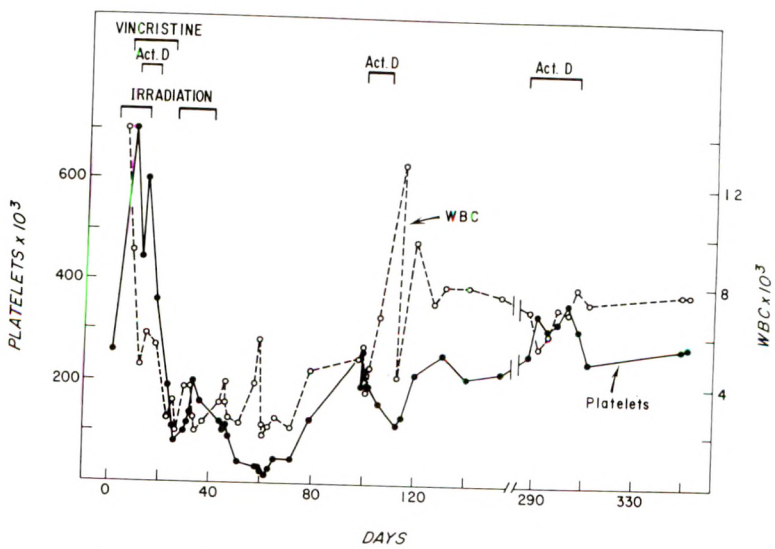


Fig. 21. Case IV. Graph relates peripheral cell counts to therapy (see text).

the irradiated right hepatic lobe and hypertrophy of the left lobe.[5,17] The liver function tests revealed some slight elevation (SGOT-80; LDH-200; alkaline phosphatase 10.6). At laparotomy, thrombosis by fibrous tissue blocked the inferior vena cava—no tumor was evident. Biopsy of a grossly contracted right lobe of the liver showed severe portal and central vein thrombosis and lobular atrophy, as expected after irradiation.[5,21] The left lobe of the liver was hypertrophied.

She remains well without evidence of tumor recurrence and without liver dysfunction. A fourth course of actinomycin D was instituted in June, 1968, without untoward reaction.

DISCUSSION

In a recent report, we have noted the lack of clinical and laboratory signs of liver dysfunction when irradiation is delivered to a portion of the intact and normal liver of a child, even when the radioisotope scan shows irregular distribution of isotope within the irradiated portion of the liver.[5] This conforms to other reports[13,31] and differs from that of Ingold *et al.*[11] where severe liver dysfunction has been reported. One might suppose that the difference lies in the volume of liver irradiated, dose delivered, and possible compromise of liver tissue by an intrinsic underlying abnormality, such as neoplastic infiltration or infection. In all of our reported cases, only a portion of the liver was irradiated, doses were lower than those reported to cause a higher incidence of liver dysfunction,[11] and no known underlying liver abnormality was present.

In a soon to be published report,[7] we will describe 2 patients who received combined irradiation and chemotherapy to the remaining volume of liver following partial hepatic resection for metastases. From that experience, we have observed marked clinical and laboratory evidence of liver failure when treatment is delivered in the immediate postoperative period and before regeneration of liver tissue is possible, even when the radiation dose does not exceed 600 rads in 4 days to 1,200 rads in 6 days. The regenerating liver seems acutely sensitive to the adverse effects of such therapy.[6,15,32]

Cases I and II are dissimilar to our previously reported cases[5] since each had had partial resection of the liver for a primary neoplasm and each underwent irradiation to the total volume of remaining liver tissue. Their relatively benign course of liver dysfunction may have been related to the period prior to initiating therapy and thus allowing some liver regeneration on the one hand,[7,8,9] and to dose of irradiation and lack of intrinsic liver abnormality on the other hand.[11]

The role of chemotherapy in these patients must be evaluated. Case I had received 5-fluorouracil, in addition to irradiation, for tumor recurrence. This drug requires a normal functioning liver for detoxification.[2,16] One may postulate that as the effects of irradiation on liver tissue were occurring, as noted by isotope scanning and liver function tests, failure of detoxification of the drug by the liver caused a more pronounced suppression of bone marrow than might have been expected.[14] Lack of unirradiated liver tissue may have accentuated this phenomenon. The relatively prompt recovery of liver function and bone marrow suppression may be related both to the low radiation dose and lack of underlying intrinsic liver abnormality.

Case II exhibited abnormal liver function tests in the immediate posthepatectomy period, and before antitumor chemotherapy and irradiation were instituted. The return towards normal of these parameters probably indicates that the dysfunction was related to postoperative edema and the process of liver regeneration. Her subsequent course under radiation therapy possibly is related to the effects of irradiation of the total volume of liver and to the administration of actinomycin D.

Actinomycin D has no known adverse effect on normal intact liver tissue where it is concentrated to a significant degree.[19,22,23,33] However, it is known to be most toxic to tissues that are mitotically active;[19,26] evidence suggests that it may

affect adversely the regenerating liver following partial hepatic resection.[10,18,24,33] Moreover, some degree of excretion of the unaltered drug is dependent on liver function.[23,43] Therefore, one may postulate that the problem in Case II was related to the adverse effect of both irradiation[15,32] and actinomycin D on the regenerating liver. Because of diminished excretion of this drug under conditions of diminished liver reserve, bone marrow toxicity may have been enhanced;[26] the problem may have been compounded if actinomycin D enhanced significantly liver dysfunction over that due to irradiation alone, causing further lack of drug excretion. The rather severe changes of liver architecture at postmortem examination, including hyaline deposition, may support this postulate.

Of interest, also, are the abnormal liver functions (Table II—Day 74) observed when clinical recovery and improved function by radioisotope scan were noted. This may be related to the severe histologic changes as noted previously; it may indicate that these tests are more sensitive parameters than clinical or roentgenologic evaluation.

The depression of peripheral blood cell counts noted in Case III, at the time of clinical liver failure and confirmed by liver scanning and hepatic arteriography as probable irradiation effect, may be related to lack of total excretion of actinomycin D—noted as a somewhat delayed effect. Bone marrow hypoplasia was compatible with drug toxicity. This had not been noted in previous cases when similar combined therapy was instituted in patients with intact liver and when only partial liver volume was irradiated to a similar dose. Possibly there was some intrinsic abnormality of liver function which increased the tendency to liver dysfunction and this may be related to the infectious process found at second laparotomy and believed to be the cause of liver dysfunction in November, 1967 (Table III—Day 180). In addition, irradiation of the left lobe of the liver, included in the portal for lung irradiation, may have compromised liver function over that noted in our other patients where only one hepatic lobe was irradiated. Possibly the cause of the dysfunction presumed to be due to "infectious hepatitis" in November, 1967, was related to the course of actinomycin D administered just prior to the onset.

The clinical course in Case IV may be related to similar factors. Her unusual depression of peripheral cell counts may be related to the fact that irradiation of the right lobe of the liver, to a high dose, also was accompanied by lower dose exposure of the left hepatic lobe as it was included in the portal for lung irradiation.

One might also postulate that in both Cases III and IV, as the right hepatic lobe had received the higher dose and was undergoing fibrosis, the left lobe developed hypertrophy, and during this very process became more sensitive to the effect of actinomycin D and irradiation discussed previously. The ability of Case III to tolerate repeated courses of actinomycin D may be related to recovery of liver function, especially the left lobe, and this is related in turn to the lower dose delivered. In both patients, hepatic arteriography, scanning, and laparotomy confirmed hypertrophy of the left lobe, and fibrosis of the right.

The diminished survival and sequestration of platelets in the spleen (Case II) may be related to the acute stage of hepatic congestion from irradiation. The altered hemodynamics of liver blood flow may lead to congestion of the portal bed and spleen with a resultant increased destruction of platelets. The normal bone marrow examination in Case II suggests that bone marrow depression from drug toxicity may not be the entire process.

Bone marrow suppression by vincristine sulfate is less marked than its neurotoxicity,[30,34] although the former is not unknown.[12] Its effect against normal liver tissue has been described;[1] its toxicity may be enhanced in cases of liver failure.[25] However, since none of our patients manifested neurotoxicity, and in view of the rare bone

marrow effect of this drug, we believe that vincristine probably was not a significant factor in these patients.

We suggest that irradiation of the total liver volume, especially after partial liver resection, be undertaken with extreme caution, especially if antitumor chemotherapy, which may require liver for detoxification or excretion, also is to be used, even when moderate doses of radiation are employed. Other previous experience indicates the importance of withholding therapy for a time to allow liver regeneration.[6,7,32] When high dose irradiation of only a portion of the liver is associated with a lower dose treatment to the remaining liver tissue, and/or if underlying liver disease is present, caution must be used. This situation appears to be dissimilar to irradiation, at high dose, of only a portion of the intact and healthy liver.[5]

SUMMARY

Four patients are described who have manifested unusual reactions to combined irradiation and chemotherapy when irradiation of the liver was involved. Two had had partial resection of the liver and irradiation of all of the remaining liver tissue; each of the others, with an intact liver, may have had compromise of liver function by infection and/or by lower dose irradiation of the left lobe of liver.

We suggest that irradiation of the liver, especially in patients who receive chemotherapeutic agents which may require liver for detoxification or excretion, be very carefully administered, even at a minimal dose. Any underlying compromise of the liver must be evaluated carefully. In each patient, hemoglobin levels were normal throughout the clinical course.

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We wish to express our appreciation to Mr. Larry Button who performed the Cr^{51} platelet survival study in Case III.

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RADIOISOTOPIC VERSUS ULTRASONIC TESTING FOR PULMONARY EMBOLISM*

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PULMONARY embolism is one of the most common causes of hospital death. The diagnostic tests for pulmonary embolism—radioisotope lung scanning, chest roentgenography, pulmonary angiography, and serum enzymes—each provide an indication of embolism. Of these the radioisotope scanning when performed with lateral as well as anteroposterior or posteroanterior projections, is probably the most helpful. In our series, most patients did not have lateral views taken and there were 3 per cent false positive and 1 per cent false negative readings.

Radioisotope scanning has two main disadvantages: (1) the patient may be too ill to be moved to the scanning machine or too ill to keep still for the time required to perform a scanning; and (2) because of the limited spatial resolution of scanning techniques, the scan provides only broad information regarding the blood flow in the lungs. Thus there is a need for a small portable instrument which can quickly provide accurate information. Such a technique has been described by Miller *et al.*[2] based on the use of ultrasound. At the Royal North Shore Hospital of Sydney, use of ultrasonic lung examination in pulmonary embolism was first investigated by Buddee *et al.*,[1] who introduced artificial emboli into sheep locating them by ultrasound. Preliminary information is presented here on the first patients studied by both isotopic and ultrasonic methods.

The principle employed is analogous to radar, using sound rather than electromagnetic waves. Ultrasonic waves travel unchanged through a uniform medium. When, however, a change in acoustic impedance, *i.e.*, a change in density or elasticity, is encountered, part of the energy of the wave is reflected and received at the transducer which doubles as transmitter and receiver. Ischemic areas of lung, produced by pulmonary emboli, have increased density over normal tissue, and this, as Miller and associates[2] suggest, is probably the cause of the echoes characteristic of an abnormal lung. The range of the equipment is limited to some 7–8 cm. due to the high attenuation of ultrasound by the air in the lungs. Hence the lungs should be examined anteriorly, posteriorly and laterally to obtain maximum coverage.

MATERIAL AND METHODS

Radioisotope scanning was performed with a Nuclear Chicago Pho Dot Mk. II scanner and 19 hole collimator using I^{131} labeled macroaggregated albumin. Ultrasonic echograms were obtained at each intercostal space of each patient using a simple portable A-Scope instrument (*i.e.*, one-dimensional detection of echoes and one-dimensional display) developed by the Commonwealth Acoustic Laboratories, Australia. The transducer, 20 mm. in diameter, operated at 2 mHz.

Thirty-one consecutive patients who were referred to the Medical Biophysics Department for radioisotope scanning for suspected pulmonary emboli were also examined by ultrasound (Fig. 1, *A* and *B*). The end of one test and the beginning of the other were separated by less than 5 minutes. Thus the state of the lungs observed in each test was the same.

RESULTS

The final diagnosis, based on all available clinical and laboratory evidence, was pulmonary embolism in 26 of the 31 patients. Radioisotope scanning gave no false posi-

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tives and 1 false negative diagnosis in this small series. The ultrasonic test gave no false positives and 4 false negatives. In 5 cases the radioisotope scan and the ultrasonic scan were contradictory. The results are detailed in Table 1.

A short discussion of the 5 cases where there was disagreement is warranted. Firstly, take the 4 cases where the radioisotope scan proved abnormal, the echograms being normal. In 3 of these cases, all tests performed, including one pulmonary angiogram, were normal, scanning showing varying degrees of reduced blood flow. For all 3, the final diagnosis was pulmonary embolism. The 1 remaining patient had further embolic episodes and all tests became abnormal. In the fifth case of disagreement, the patient showed a false-negative radioisotope scan with abnormalities occurring on chest roentgenograms and echograms.

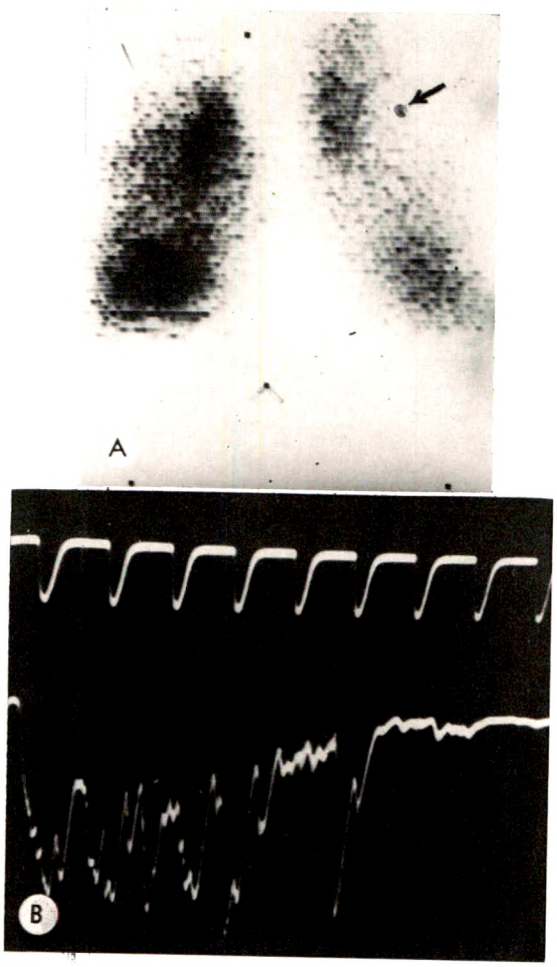


Fig. 1. (*A*) I^{131} MAA radioisotope scan and (*B*) ultrasonic echogram of a patient with proven pulmonary embolism. Arrow points to the area where the echogram shown in *B* was performed.

In this study, 5 patients were seen more than once, one having 5, another having 3 and 3 others 2 isotope scans and echograms. From these patients it appears that the echograms may remain quite abnormal while the isotope scans are resolving. Wolfe and Sabiston[3] found that lung isotope scans can show a return to normal while the clot causing embolism is still in place. It seems logical that an echogram, relying purely on changes in acoustic impedance, would remain abnormal while a clot remains. This is important in determining the progress of a patient who has suffered from pulmonary embolism.

The patients presented as having pulmonary embolism had no other lung disorders at the time of examination. This choice was deliberate, as not enough patients having emphysema, bronchitis, etc., have been examined to enable the effect on the echogram to be predicted. However, the few patients studied have shown positive scans in the presence of atelectasis and bronchitis. In addition, it appears that an echogram of a patient with a large pleural effusion will pick up both walls of the lung due to the decrease in aeration, and the subsequent increase in range of the instrument.

DISCUSSION

In performing and interpreting a lung echogram, great care must be taken to avoid spurious results. The positioning of the transducer, provision of a good transducer/skin interface, adjustment of the instrument controls, etc., are critically important, and the operator must have a knowledge of the physical ultrasonic principles involved to accurately perform and read an echogram. Echoes of small amplitude are generally spurious.

TABLE I

COMPARISON OF RADIOISOTOPE AND ULTRASONIC TESTING FOR PULMONARY EMBOLISM

Patient No.	Radioisotope Scan	Ultrasonic Echogram	Final Diagnosis
1	Abnormal	Normal	Pulmonary embolism
1 (a)	Abnormal	Abnormal	Resolving pulmonary embolism
1 (b)	Abnormal	Abnormal	Resolving pulmonary embolism
2	Abnormal	Abnormal	Pulmonary embolism
3	Abnormal	Abnormal	Pulmonary embolism
4	Normal	Normal	Not pulmonary embolism
5	Normal	Abnormal	Pulmonary embolism
6	Normal	Normal	Not pulmonary embolism
7	Abnormal	Abnormal	Pulmonary embolism
8	Abnormal	Abnormal	Pulmonary embolism
8 (a)	Abnormal	Abnormal	Resolving pulmonary embolism
8 (b)	Abnormal	Abnormal	Resolving pulmonary embolism
8 (c)	Abnormal	Abnormal	Resolving pulmonary embolism
8 (d)	Abnormal	Abnormal	Resolving pulmonary embolism
8 (e)	Abnormal	Abnormal	Resolving pulmonary embolism
9	Abnormal	Abnormal	Pulmonary embolism
10	Abnormal	Normal	Pulmonary embolism
11	Abnormal	Abnormal	Pulmonary embolism
12	Abnormal	Abnormal	Pulmonary embolism
13	Abnormal	Abnormal	Pulmonary embolism
14	Abnormal	Abnormal	Pulmonary embolism
14 (a)	Abnormal	Abnormal	Resolving pulmonary embolism
15	Abnormal	Abnormal	Pulmonary embolism
16	Normal	Normal	Not pulmonary embolism
17	Abnormal	Abnormal	Resolving pulmonary embolism
18	Abnormal	Normal	Pulmonary embolism
19	Abnormal	Abnormal	Pulmonary embolism
20	Normal	Normal	Normal
21	Normal	Normal	Normal
22	Abnormal	Abnormal	Pulmonary embolism
22 (a)	Abnormal	Abnormal	Resolving pulmonary embolism
23	Abnormal	Abnormal	Pulmonary embolism
24	Abnormal	Abnormal	Pulmonary embolism
25	Abnormal	Abnormal	Pulmonary embolism
26	Abnormal	Abnormal	Pulmonary embolism
27	Abnormal	Normal	Pulmonary embolism
27 (a)	Abnormal	Abnormal	Resolving pulmonary embolism
28	Abnormal	Abnormal	Pulmonary embolism
29	Abnormal	Abnormal	Pulmonary embolism
30	Abnormal	Abnormal	Pulmonary embolism
31	Abnormal	Abnormal	Pulmonary embolism
True Positive	35	32	
False Positive	0	0	
True Negative	5	5	
False Negative	1	4	

Anterior examination of the superior lobes of the lung and areas near the mediastinum can give false positive results.

It is anticipated that as experience is accumulated, the error rate will fall and quantitative information regarding the depth of a suspected embolus may be used. Ultrasonic echograms and radioisotope

scans should prove powerful complements in the diagnosis of pulmonary embolism.

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PULMONARY PHOTOSCAN–ROENTGENOGRAPHIC COMPARISONS IN SARCOIDOSIS*

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PROGRESSIVE impairment of pulmonary function is the leading cause of morbidity and mortality in sarcoidosis.[7,9,13] Detection and quantitation of this functional deficit is one requisite for rational application and evaluation of therapy.

There has been a tendency in the past to relate the pulmonary functional status of the patient with sarcoidosis to chest roentgenographic findings. This relationship is at least implicit in attempts to classify pulmonary involvement in sarcoidosis on the basis of roentgenographic patterns. [7,12,13] There are many studies, however, which have demonstrated a poor correlation between the chest roentgenogram and the clinical, pulmonary functional and pathologic findings.[6,8,12] Indeed, the chest roentgenogram has been notoriously deceptive in reflecting the functional status of the patient.[16,19]

Spain[15] has emphasized that the pulmonary functional deficit in sarcoidosis is dependent upon the location, rather than the extent, of fibrosis in the lungs. He has described 5 patterns of pathologic involvement: bronchial, interstitial, parenchymal, vascular and pleural. The pulmonary vascular bed can be involved in several of these patterns. More recently, Thompson[17] has emphasized the frequency and potential functional importance of pulmonary vascular involvement in sarcoidosis.

Such considerations suggest that the detection of abnormalities in pulmonary blood flow may provide a more sensitive guide to functional impairment in sarcoidosis than does the chest roentgenogram. The pulmonary photoscan has been established as a safe, reliable and simple method for assessing alterations in the distribution of pulmonary blood flow.[18] We have, therefore, performed lung photoscans in patients with sarcoidosis and have correlated the photoscan findings with the roentgenographic patterns. The data accumulated indicate that the photoscan does provide information not available from the roentgenogram.

MATERIAL AND METHOD

Thirty-one patients with sarcoidosis seen at the Pulmonary Disease Division, Georgetown University Hospital, were included in this study. All met the criteria of the International Congress on Sarcoidosis for the diagnosis of sarcoidosis;[11] a compatible clinical picture plus histologic evidence of noncaseating granuloma. Their evaluation included history and physical examination, complete blood cell count, urinalysis, blood urea nitrogen, serum calcium and phosphorus, liver function studies and serum protein electrophoresis plus quantitation of immune globulins. In addition, chest roentgenography, complete pulmonary function studies including arterial blood gases, skin tests, bacteriologic and fungal studies, ophthalmologic evaluation and appropriate biopsies were done.

Perfusion lung scannings were performed utilizing radioiodinated macroaggregated albumin (I^{131} MAA); 400 μc was injected intravenously, 200 μc in the prone position and 200 μc in the supine position. Early in the study, scannings were done with a rectilinear scanner; later, with the Anger scintillation camera.[1] Rectilinear scannings were performed in the anteroposterior and posteroanterior projections. Scintillation scannings were done in the anteroposterior, posteroanterior and both lateral projections.

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Thirty-eight scannings were performed in 31 patients: 25 patients had a single scanning; 4 had an initial scanning and 1 follow-up; and 1 patient had an initial scanning and 2 follow-up scannings. All scannings were done within a few days of the chest roentgenography with which they were compared. Arbitrary classifications of the roentgenograms and scans were prepared and are listed in Tables I and II. Representative examples of each classification are demonstrated in Figures 1, *A–D* and 2, *A-D*.

Lung scans and chest roentgenograms were assigned random numbers, so that there was no correlation between individual roentgenograms and scans. Classification of each roentgenogram and scan then was made independently by three qualified observers. The final classification assigned to the roentgenogram and lung scan of each patient was an arithmetic mean of the 3 interpretations. Finally, the roentgenographic and scan classifications for each patient were compared.

RESULTS

The classification of each roentgenogram and scan in the 31 patients is presented in Table III. In general, correlation between them was unreliable. Figure 3 illustrates a composite of the scan/roentgenogram classifications for each of the 38 scan/roentgenogram pairs. Roentgenograms were more abnormal than scans in 21 instances (55.3 per cent), while scans were more abnormal than corresponding roentgenograms in 10 instances (26.5 per cent). In 7 scan/roentgenogram pairs (18.3 per cent), classification was identical.

Table I

CLASSIFICATION OF CHEST ROENTGENOGRAMS

Group I	Normal except for hilar lymphadenopathy
Group II	Hilar lymphadenopathy plus minimal parenchymal stranding, usually in perihilar areas
Group III	Prominent parenchymal infiltration and/or nodularity without evidence of significant fibrosis, retraction, cyst formation, or honeycombing
Group IV	Parenchymal infiltration and/or nodularity with significant fibrosis, retraction, cyst formation, or honeycombing

Table II

CLASSIFICATION OF LUNG SCANS

Group I	Normal scan with or without defects confined to the hilar regions
Group II	Uneven distribution of radioactivity without definite "cold" areas
Group III	Uneven distribution of radioactivity with clear-cut "cold" zones whose area is less than one-third of a single lung field
Group IV	Total area of "cold" zones exceeds one-third of a single lung field

Statistical analysis of the classifications disclosed that the mean "rank" for roentgenograms was 2.5 (S.D. $\pm$1.0) and for photoscans, 2.3 (S.D. $\pm$0.9). Application of the "t" test disclosed that the difference between mean ranks was not statistically significant; however, more meaningful was the fact that the correlation coefficient relating scan to roentgenographic rank was low ($r = 0.308$). This provides mathematical confirmation of the unreliable correlation graphically depicted in Figure 3.

Examples of the roentgenogram/scan results in several representative cases are presented in Figure 4, *A* and *B*; 5, *A* and *B*; and 6, *A* and *B*. The patient depicted in Figure 4, *A* and *B* had a strikingly abnormal roentgenogram, while the scan showed minimal derangement of pulmonary blood flow. Figure 5, *A* and *B* demonstrates a roentgenogram and scan in a patient in whom the 2 were comparable. Figure 6, *A* and *B* is an instance in which the scan disclosed extensive alterations in pulmonary blood flow not suggested by the roentgenogram.

DISCUSSION

It has been generally accepted that among the standard parameters previously available for investigation of patients with pulmonary involvement due to sarcoidosis (clinical features, chest roentgenography, pulmonary function tests, pathologic examination), the best correlation existed be-

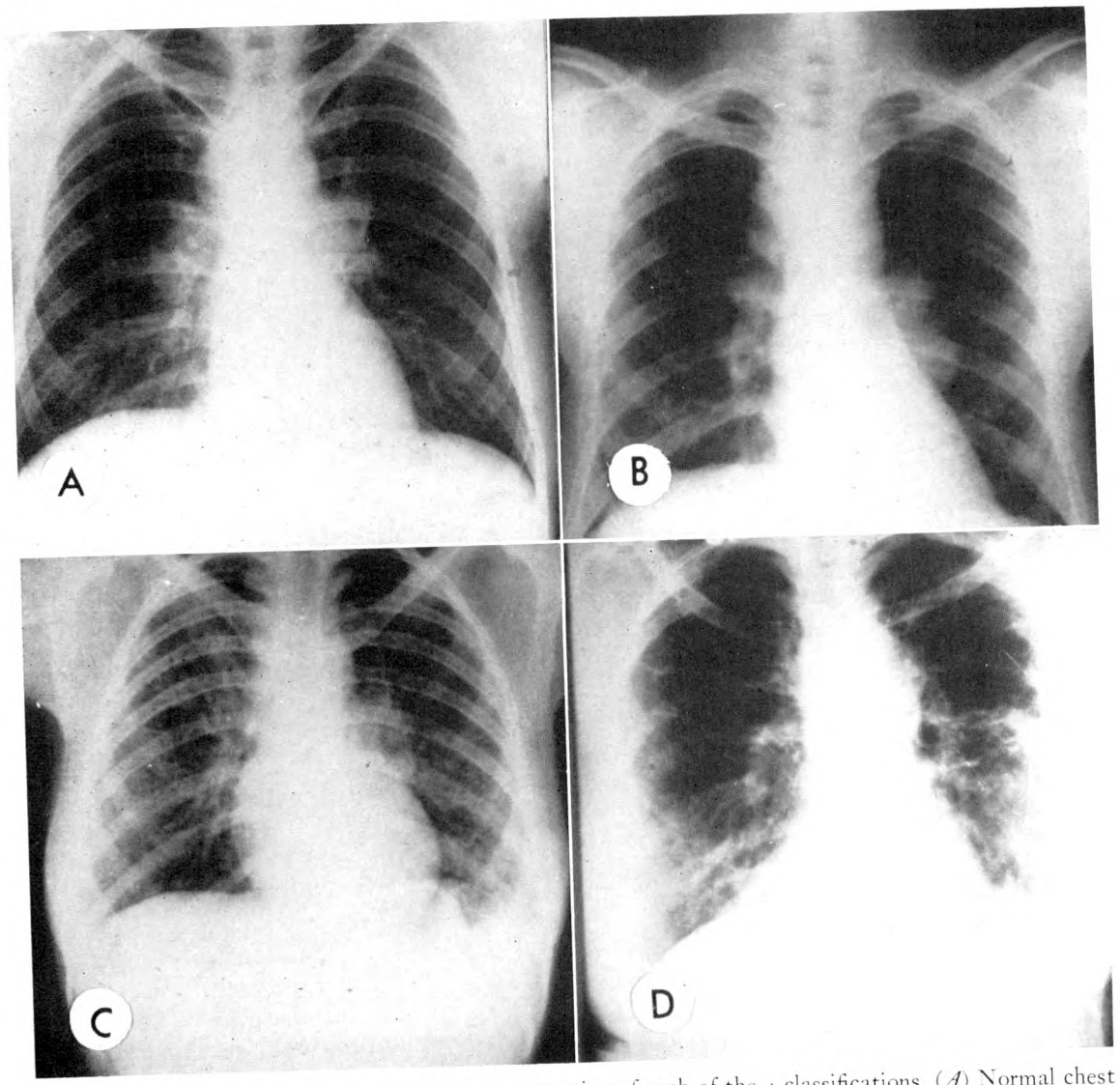


FIG. 1. Examples of chest roentgenograms representative of each of the 4 classifications. (*A*) Normal chest except for the presence of hilar and paratracheal lymphadenopathy. (*B*) Hilar and paratracheal lymphadenopathy with minimal perihilar infiltration. (*C*) Mediastinal lymphadenopathy and a diffuse, bilateral parenchymal infiltration. (*D*) Marked fibrosis, honeycombing and cyst formation.

tween pulmonary function and microscopic examination of the lung.

As mentioned above, Spain[15] has indicated that the precise functional deficit depends upon the anatomic distribution of the sarcoid granulomata and/or fibrosis. McClement *et al.*,[10] Gray and Gray[4] and others[6] have presented the patterns of ventilation and gas exchange abnormalities which result in various degrees of pulmonary disability and have suggested that there is good pathophysiologic correlation.

On the other hand, Bates and Christie,[2] Sharma *et al.*,[14] Boushy *et al.*,[3] and others[5] recently have stressed the poor correlation between pulmonary function and roentgenographic appearance. Their studies have disclosed that functional abnormalities may be present in the absence of, or even after the disappearance of, recognizable roentgenographic abnormalities. In the early stages of pulmonary parenchymal sarcoidosis, granulomata may be present in interstitial, peribronchial, subpleural, perivascu-

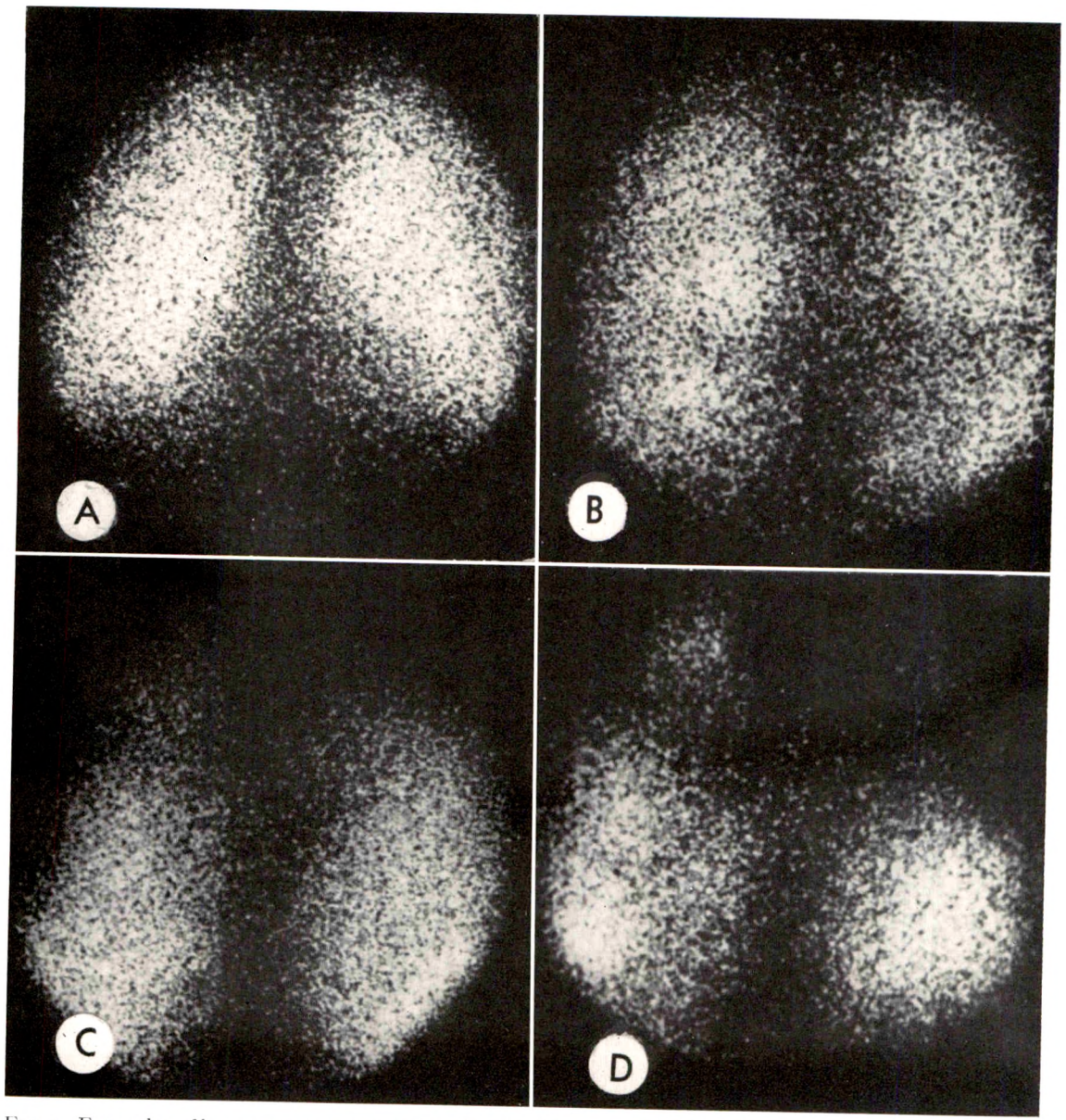


Fig. 2. Examples of lung scans representative of each of the 4 classifications. (*A*) Anteroposterior projection. (*B*, *C* and *D*) Posteroanterior projections. (*A*) Normal lung scan. (*B*) Bilateral patchy zones of decreased activity. (*C*) Clear-cut "cold" zone in apex of right lung and area of decreased activity in left apex. (*D*) Bilateral "cold" zones, and patchy areas of decreased activity. Abnormal areas comprise more than one-third of a single lung field.

lar, or intra-alveolar regions. It is not only the extent of this pathologic process, but the strategic location of the lesions that accounts for the type and degree of functional impairment. Neither the extent nor the histologic location of the lesions is accurately reflected on the chest roentgenogram. Thus, the poor correlation between roentgen appearance and pulmonary functional status is not surprising.

Our data reveal that roentgenogram/scan correlation was inconsistent and unreliable. In many instances, the visual appearance of the chest roentgenogram was significantly worse than the scan. Even more intriguing were those cases in which

TABLE III

CLASSIFICATION OF ROENTGENOGRAMS AND SCANS

Patient No.	Age	Sex	Race	Roentgenographic Classification	Scan Classification	Roentgenogram Scan Classification Difference
1	24	F	N	1.0	1.0	0
				3.3	3.0	0.3
2	44	M	N	4.0	1.6	2.4
3	26	F	N	2.0	1.3	0.7
				2.0	1.0	1.0
4	35	M	N	1.0	1.0	0
5	19	M	N	2.3	3.0	0.7
6	27	F	N	1.6	2.0	0.4
7	35	F	N	4.0	2.0	2.0
8	25	F	N	3.6	3.0	0.6
9	23	F	N	2.6	2.3	0.3
10	13	M	W	2.0	1.0	1.0
11	23	F	W	1.3	1.0	0.3
12	44	F	N	4.0	3.0	1.0
13	37	M	N	2.3	1.6	0.7
				2.3	1.6	0.7
14	40	M	N	4.0	3.6	0.4
15	37	F	N	3.0	4.0	1.0
				3.0	2.6	0.4
16	17	F	N	3.0	2.3	0.7
17	37	M	W	4.0	2.0	2.0
18	22	M	N	3.0	1.3	1.7
19	26	F	N	1.6	2.3	0.7
20	23	F	N	3.0	3.0	0
21	31	M	N	3.3	2.6	0.7
22	31	F	N	4.0	3.0	1.0
23	22	M	W	2.0	2.0	0
24	28	M	N	2.0	3.3	1.1
25	32	F	N	2.6	2.0	0.6
26	26	F	N	2.0	2.0	0
				2.6	1.6	1.0
				1.3	2.3	1.0
27	22	M	N	1.0	4.0	3.0
				1.0	3.0	2.0
28	55	F	N	2.3	2.3	0
29	37	M	W	1.0	2.0	1.0
30	39	F	N	4.0	4.0	0
31	17	M	W	2.0	4.0	2.0

the scan was quite abnormal while the roentgenogram was essentially normal (except for hilar lymphadenopathy).

The basic pathologic process in pulmonary sarcoidosis is an evolution from multiple granulomata to healing, with or without significant fibrosis. Pulmonary blood flow may be affected in several ways. There may be direct granulomatous infiltration of vessel walls—an occurrence which may be more frequent than formerly supposed. More commonly, it is fibrosis which leads to obliteration of the vascular bed. Finally, pathologic involvement of bronchial, alveolar, or interstitial areas may produce zones of impaired ventilation, leading to regional hypoxia and resultant vascular constriction.

It may be that a key determinant of significant pulmonary functional impairment is the extent and location of vascular involvement. The lung scanning is a reliable method for providing both a qualitative visual presentation and a quantitative measure of regional pulmonary blood flow.[18] That it can detect the presence of functionally significant pulmonary parenchymal disease more accurately than chest roentgenography seems apparent. We are currently investigating the possibility, therefore, that the photoscan may also correlate more closely with pulmonary functional status.

Certainly, the lung scan provides a new dimension in the assessment of pulmonary involvement in sarcoidosis and represents a valuable addition to standard techniques employed in the study of this bewildering disease. It has already provided some fresh insights and may serve as a valuable procedure in the initial and long term evaluation of the patient with sarcoidosis.

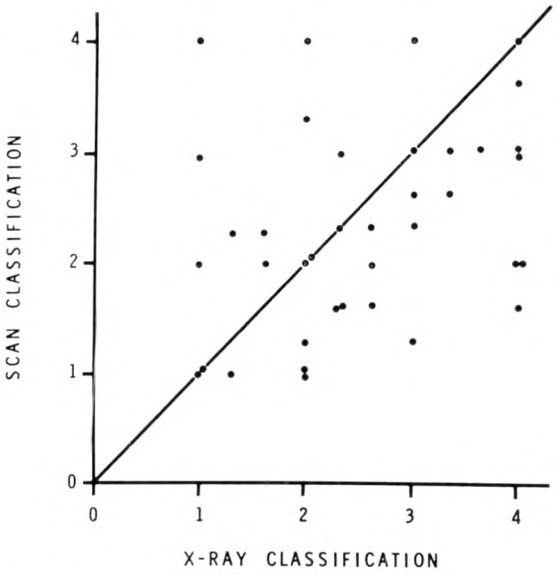


Fig. 3. Composite of classifications of 38 roentgenogram/scan pairs in 31 patients. Roentgenographic classifications are plotted on the abscissa, scan classifications on the ordinate. Points falling on the line of identity represent instances in which classifications are identical. Points above the line are those instances in which scans were more abnormal than roentgenograms; points below, instances in which roentgenograms were more abnormal than scans.

SUMMARY

Several patterns of roentgenographic and functional abnormalities occur in patients with pulmonary sarcoidosis. Little correlation exists between the roentgenographic appearance and functional impairment. The histologic location of lesions is the determinant in the kind and severity of func-

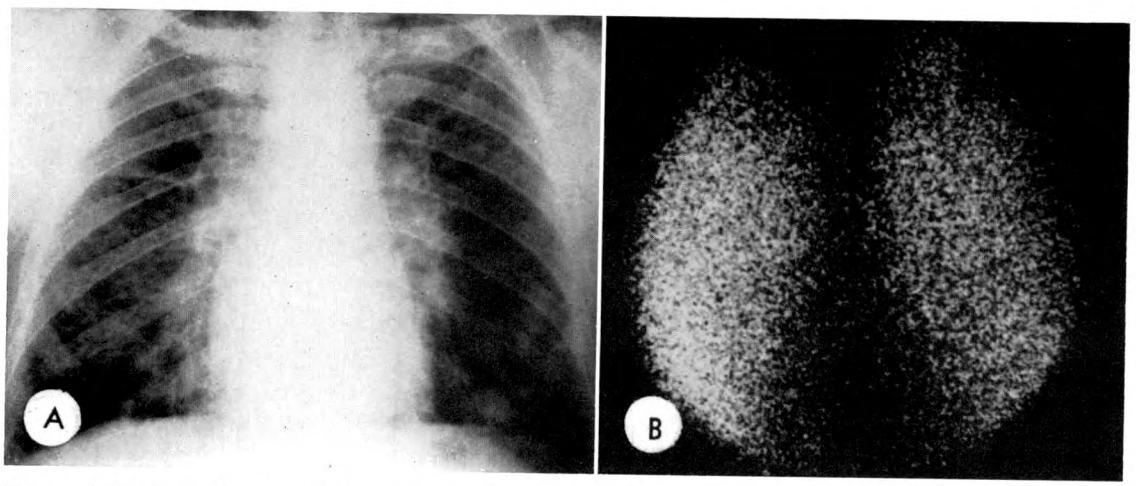


Fig. 4. (*A* and *B*) Chest roentgenogram and lung scan obtained on patient No. 18. Chest roentgenogram reveals bilateral diffuse nodular infiltration and mediastinal lymphadenopathy (Class III). Lung scan (anteroposterior projection) is within normal limits (Class I). Apparent disparity in activity between the 2 lungs is an artifact.

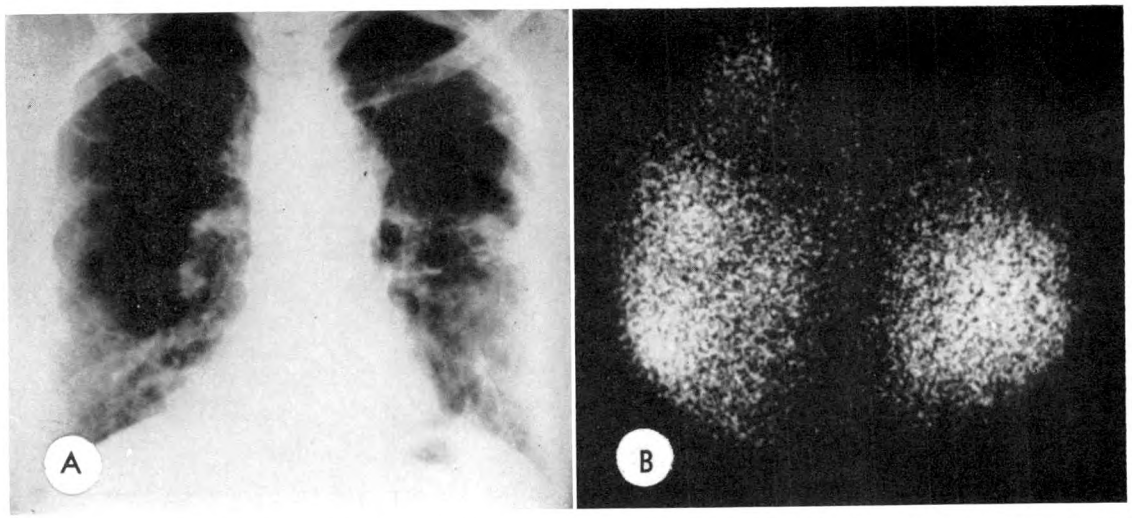


FIG. 5. (*A* and *B*) Chest roentgenogram and lung scan obtained on patient No. 30. Chest roentgenogram reveals diffuse fibrocystic disease. Scan (posteroanterior projection) reveals large "cold" areas in both apices with mottled defects in lower lung fields. Both roentgenogram and scan are Class IV.

tional abnormality, and may not be accurately reflected by the chest roentgenogram.

The pulmonary vascular bed may be involved either primarily or secondarily. The radioactive lung scanning is a technique for assessing pulmonary blood flow distribution.

This study was undertaken to examine the role of the scanning in the evaluation of 31 patients with pulmonary sarcoidosis. Chest roentgenograms and scans in each patient were classified and compared. Poor correlation existed between roentgenographic and scan classifications.

These studies indicate that the lung scan

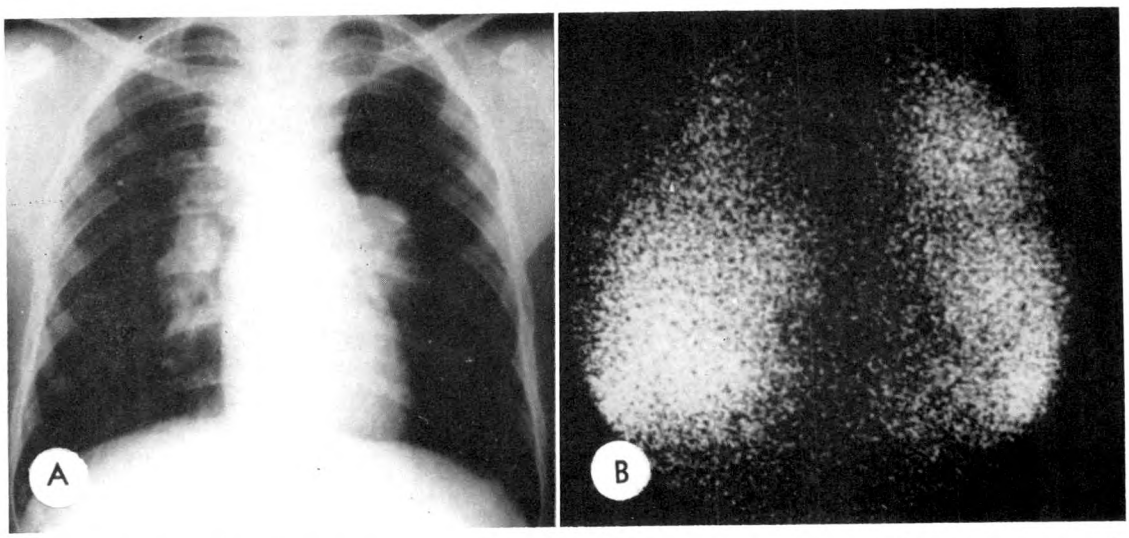


FIG. 6. (*A* and *B*) Chest roentgenogram and lung scan obtained on patient No. 27. Chest roentgenogram is normal except for hilar and paratracheal lymphadenopathy (Class I). Lung scan (posteroanterior projection) reveals significantly decreased activity in both upper lobes and patchy defects in the right lower lobe (Class IV).

reflects the vascular component of pulmonary parenchymal involvement more accurately than the chest roentgenogram. Studies are underway to determine whether it correlates more closely with pulmonary function than the chest roentgenogram.

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SCINTIGRAPHIC FINDINGS IN PULMONARY MICROEMBOLISM*

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THE frequency and clinical importance of pulmonary embolism have been repeatedly emphasized in recent medical publications.[5,11] The condition has numerous manifestations and an understanding of the pathophysiology, diagnostic criteria and therapeutic management for its different forms is currently incomplete. Several communications have recently dealt with the problem of pulmonary microembolism.[2,8,9] While the roentgenologic manifestations of pulmonary infarction and pulmonary "macroembolism" have been described, the roentgenographic, angiographic, and scintigraphic findings in microembolism have received little attention. This report describes a scintigraphic pattern (initially noted by M.S.P.) which appears to reflect the effects of multiple pulmonary microemboli.

MATERIAL AND METHODS

Roentgenologic, pathologic and experimental material have been utilized in the synthesis of this presentation.

1. *Pulmonary Scintigraphy.* Several hundred lung scintigraphies performed on patients clinically suspected of having pulmonary embolic disease were reviewed. The radiopharmaceutical employed was I^{131} labeled macroaggregated albumin. An Anger scintillation "camera" was used as the imaging device.[1]

2. *Experimental Pulmonary Microembolism.* Pulmonary microembolism can be produced in dogs by intravenously administering polystyrene microspheres of preselected size.[6] Thereafter, pulmonary scintigraphy and/or postmortem pulmonary angiography can be performed and the results correlated with the distribution of microemboli in the lungs. A program of investigation along these lines is currently underway in our laboratory, and technical details are described in a separate communication.[7]

3. *Human Postmortem Pulmonary Arteriography.* Large numbers of postmortem pulmonary arteriographies have been performed at the Peter Bent Brigham Hospital since 1960.[11] Access to this material was graciously given to us by Drs. Gustave J. Dammin and George T. Smith. We reviewed the arteriographic findings and correlated selected patterns with the reported histologic findings. Technical details concerning actual performance of postmortem pulmonary arteriography are described in the publication referred to immediately above.

RESULTS

1. *Pulmonary Scintigraphy.* The scintigraphic representation of a normal lung reveals regularly distributed radioactivity throughout both lung fields (Fig. 1). In frontal projections the heart, mediastinum, and often the hili are visualized as areas where radioactivity is absent. The interlobar fissures are not normally apparent in either frontal or lateral projections.

Pulmonary "macroemboli" produce de-

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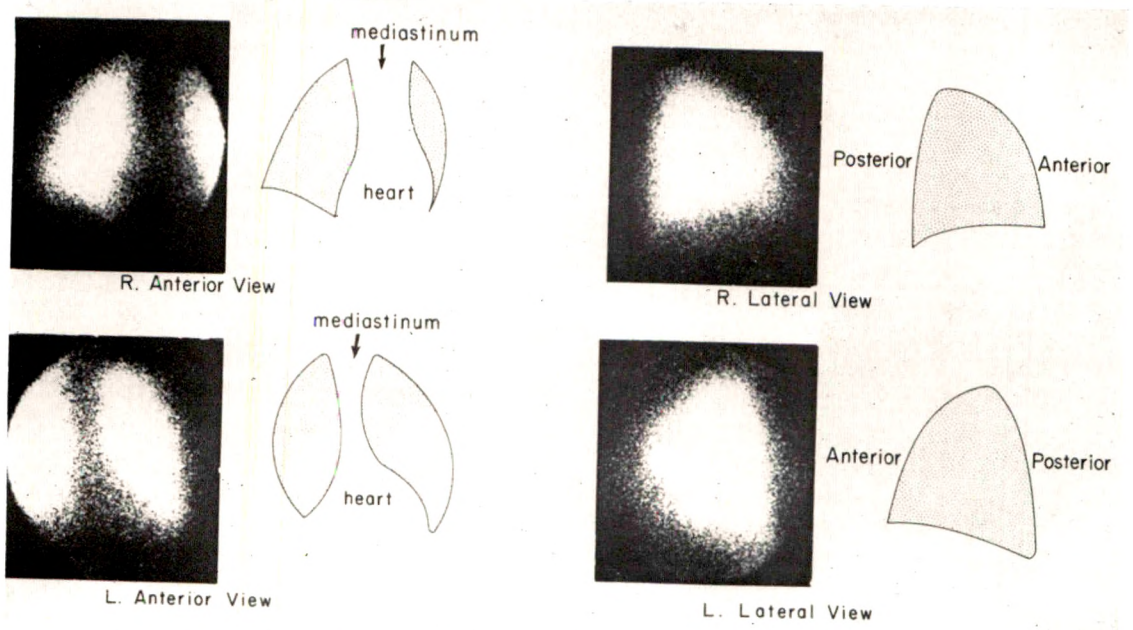


Fig. 1. Normal lung. Radioactivity is regularly distributed throughout both lung fields.

creased radioactivity in the area served by the involved artery. Large emboli produce effects in entire lobes or segments (Fig. 2); somewhat smaller emboli produce crescent-shaped areas which extend to the periphery of the lung and are pleural-based (Fig. 3). Both of these patterns correspond to diminished perfusion in the area normally fed by an embolically obstructed artery. This relationship has been repeatedly demonstrated, both experimentally and in clinical material.

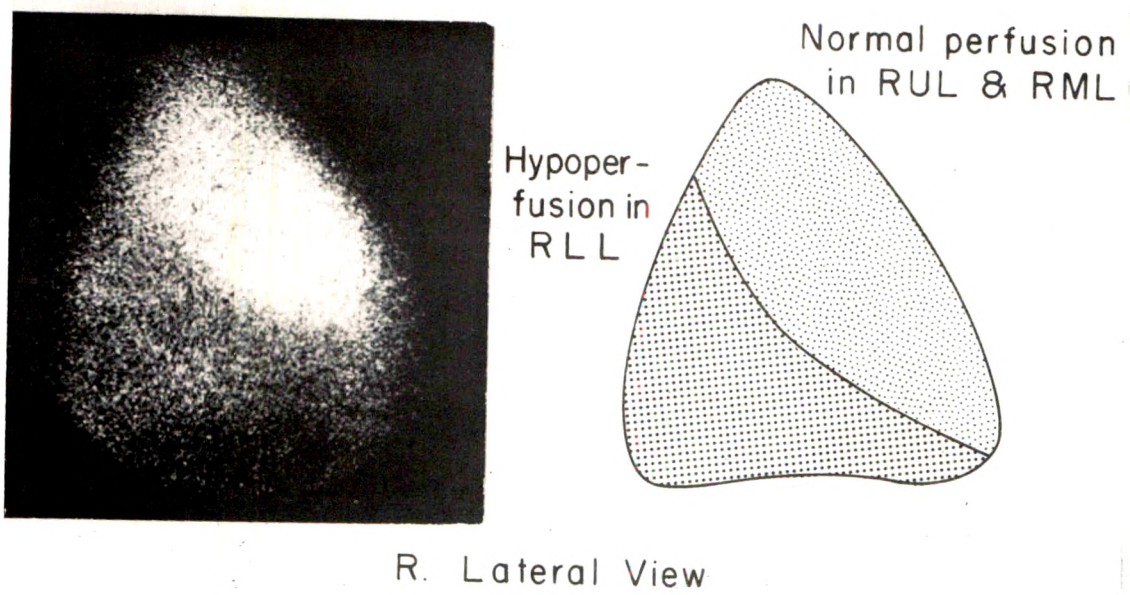


Fig. 2. Large emboli produce effects in entire lobes or segments. RLL = right lower lobe; RML = right middle lobe; RUL = right upper lobe.

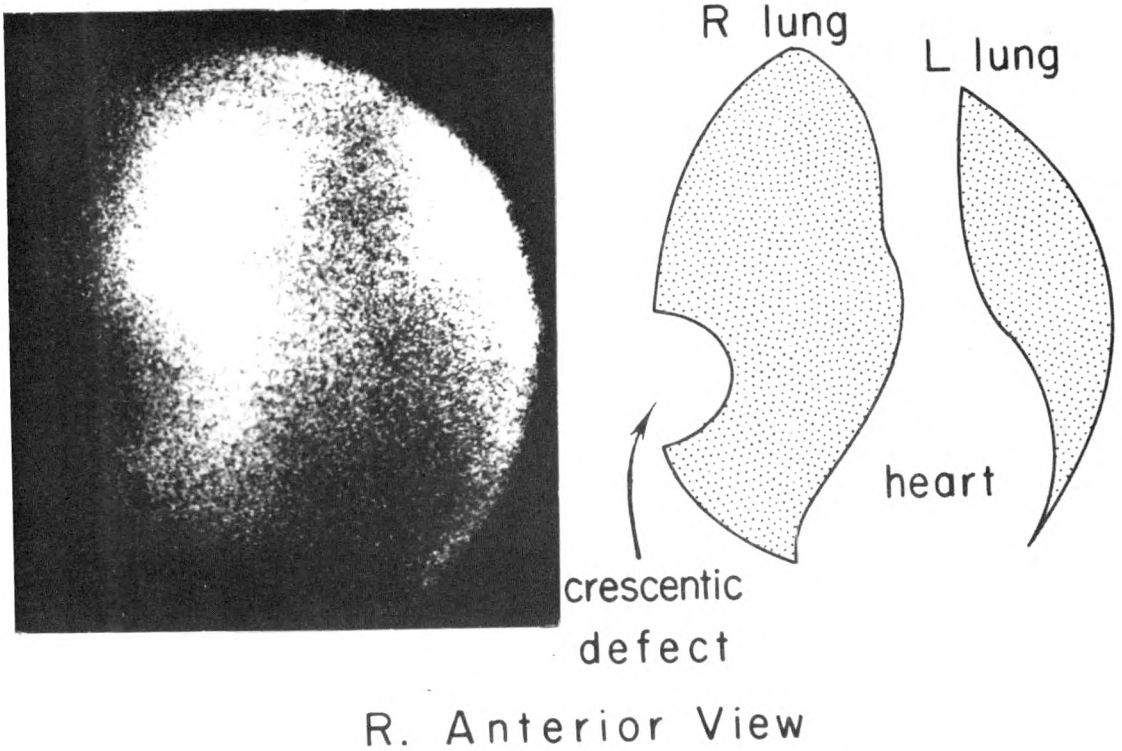


FIG. 3. Smaller emboli produce crescent-shaped areas extending to the lung periphery.

In our scintigraphic studies a different pattern has been frequently observed in patients with convincing clinical evidence for pulmonary embolism. The pattern has two components: first, there is decreased radioactivity in a distribution which corresponds to the position of an interlobar fissure (Fig. 4 and 5). We have termed this finding "fissural visualization." Secondly, there is often diminution in the apparent size of the lobe or lobes involved (Fig. 6 and 7), giving the appearance of a "shrunken lobe."

The scintigrams chosen for illustration are from patients whose concurrent chest roentgenograms were free from abnormalities such as atelectasis, consolidation, or significant pleural effusion which might have accounted for the scintigraphic defects noted. All the patients had strong clinical and laboratory evidence for pulmonary embolism. In the patients who came to postmortem examination shortly after the performance of lung scanning, multiple small emboli were found in the region of lung shown to be abnormal on the scintigrams.

2. *Experimental Pulmonary Microembolism.* Postmortem pulmonary arteriography performed on a normal dog shows that the pulmonary arteries extend out to the periphery of the lung (Fig. 8). If, in a similar dog, multiple polystyrene beads, about 1 mm. in diameter, are administered intravenously and postmortem pulmonary arteriography then performed, the periphery of the lung is seen to be ischemic, but the central portion of the lung remains relatively well perfused (Fig. 9).[6]

3. *Human Postmortem Pulmonary Arteriography.* Postmortem pulmonary arteriograms in human patients with normal lungs reveal vessels extending to the periphery of the lungs (Fig. 10). In patients found at autopsy to have multiple microemboli, the periphery of the lungs becomes ischemic while the central zone remains relatively well perfused (Fig. 11). In some instances

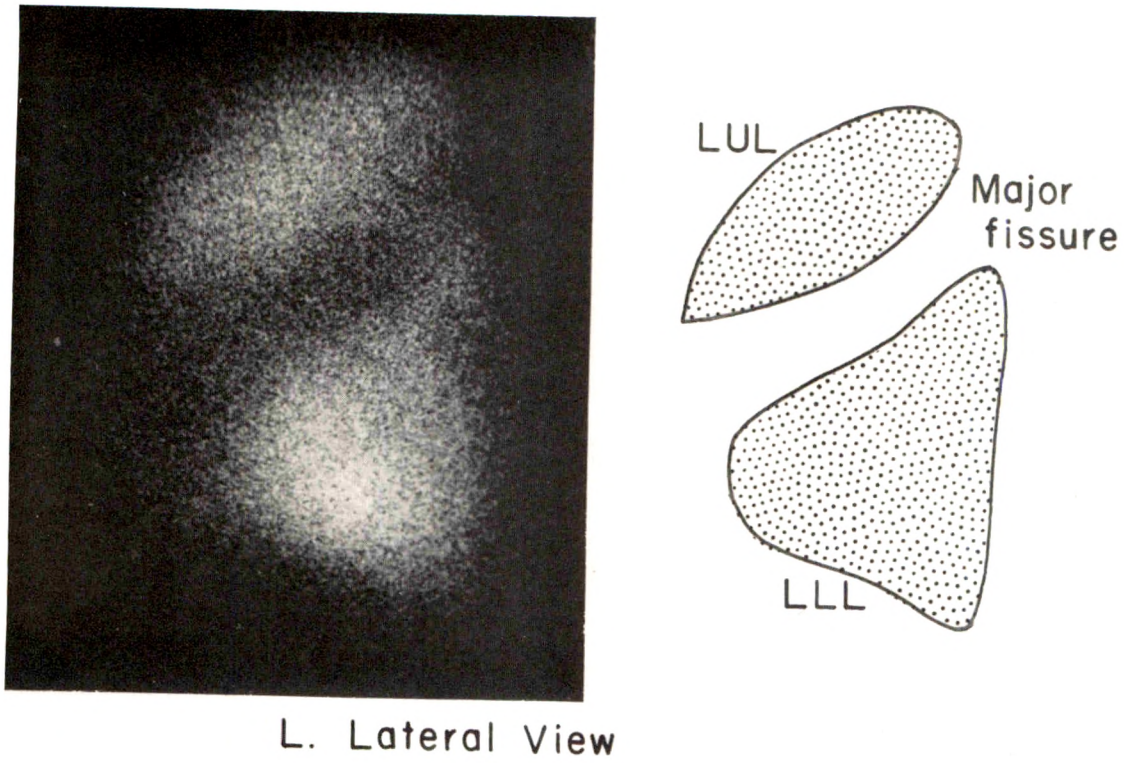


Fig. 4. Decreased radioactivity along left interlobar fissure. LLL=left lower lobe; LUL=left upper lobe.

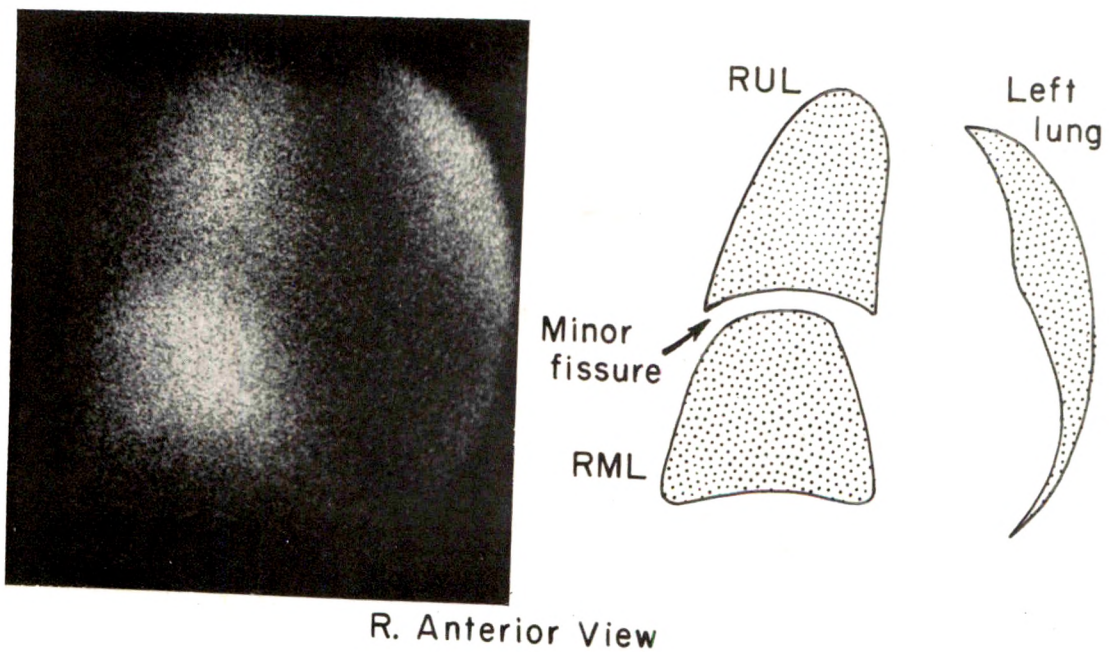
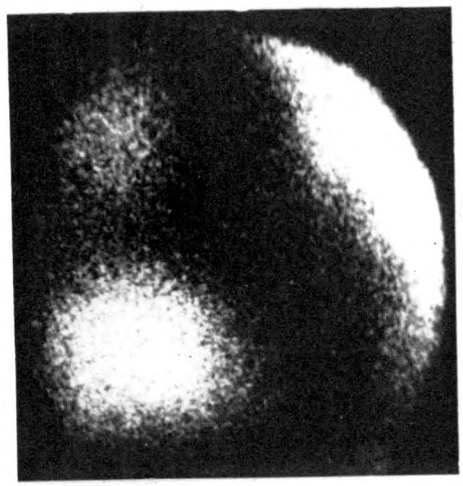
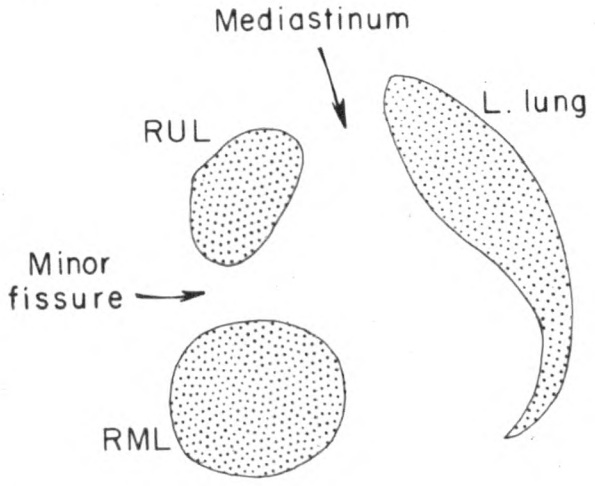


Fig. 5. Decreased radioactivity along minor fissure.

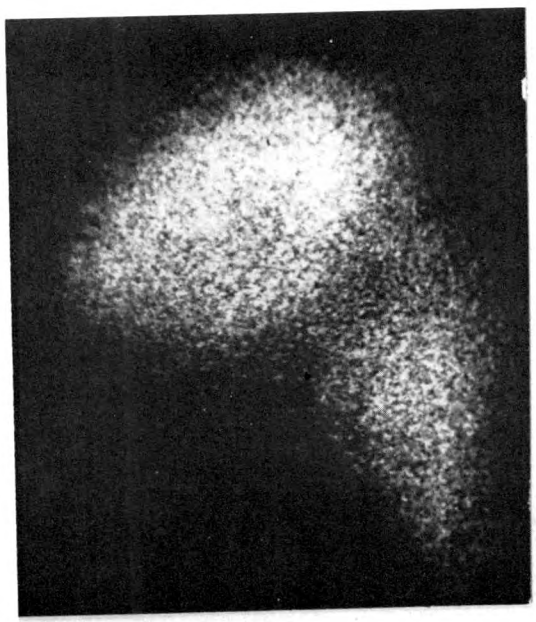


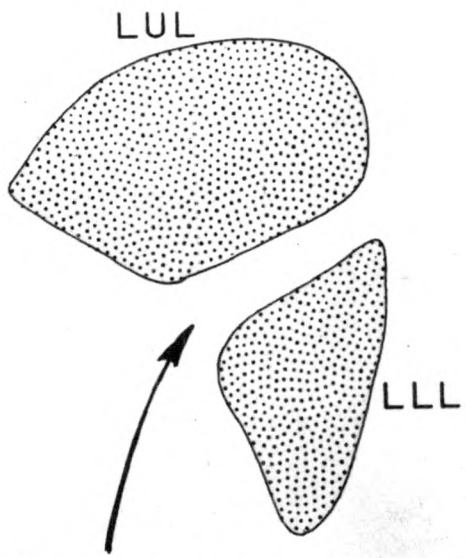


Perifissural accentuation of generalized circumferential ischemia in R. lung (especially RUL)

R. Anterior View

Fig. 6. The right upper lobe appears "shrunken."





Perifissural accentuation of circumferential LLL ischemia

Fig. 7. The left lower lobe appears "shrunken."

the peripheral zone of hypoperfusion is restricted to a single lobe.

An additional pathologic (and arteriographic) finding occasionally observed in patients with multiple microembolism is the development of collateral circulation between the bronchial and pulmonary arteries.[12] The collateral channels are arranged around the periphery of the lung (Fig. 12).

DISCUSSION

The pulmonary arteries ramify through more than 20 orders of successive branchings from the hili to the periphery of the lung. Two types of branches occur: *axial arteries* course rather directly toward the periphery of the lungs, whereas *side branches* arise at acute angles from the axial arteries to supply the more central portion of each lobe.[4,10] We have observed that small emboli tend to lodge preferentially in the peripheral axial arteries after intravenous administration. These conditions constitute the pathologic basis for peripheral ischemia in pulmonary microembolism—there is a selective decrease in blood flow to the periphery of the lung, while the central portion remains relatively well perfused.

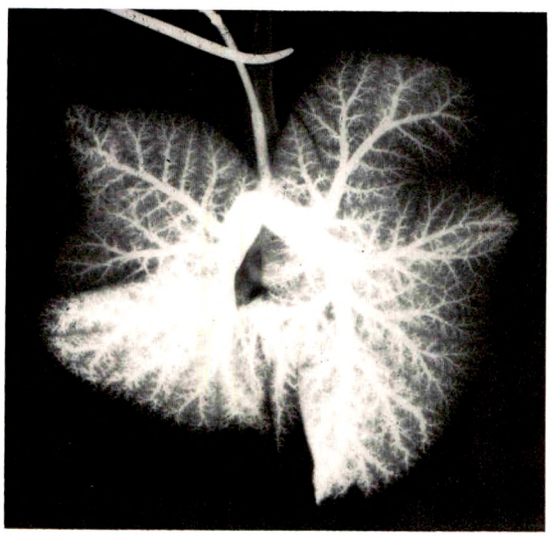


Fig. 8. Postmortem pulmonary arteriogram in control dog—pulmonary arteries extend to periphery of lung.

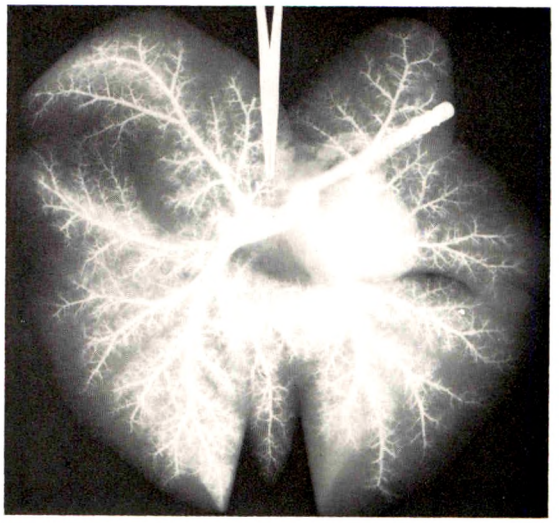


Fig. 9. Postmortem pulmonary arteriogram in microembolized dog—periphery of lung is ischemic.

Given the existence of peripheral ischemia, how might this be related to the scintigraphic abnormalities "fissural visualization" and the "shrunken lobe" which

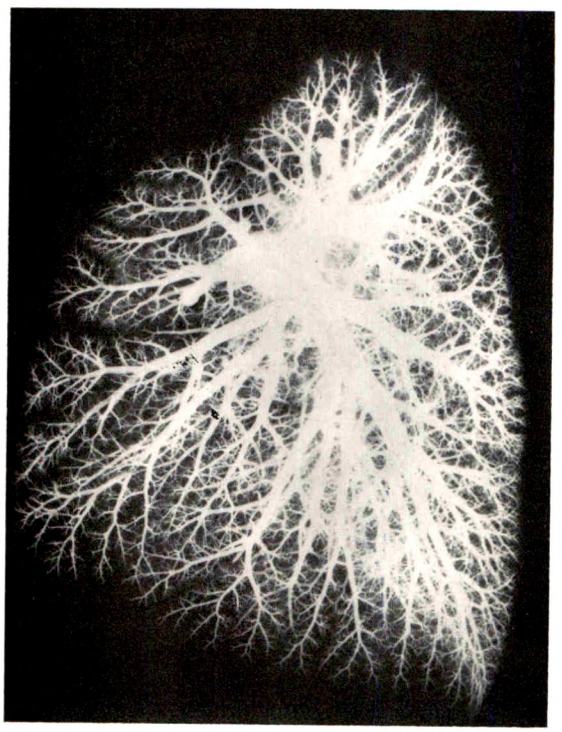


Fig. 10. Postmortem pulmonary arteriogram in human with normal lungs—pulmonary arteries extend to periphery of lung.

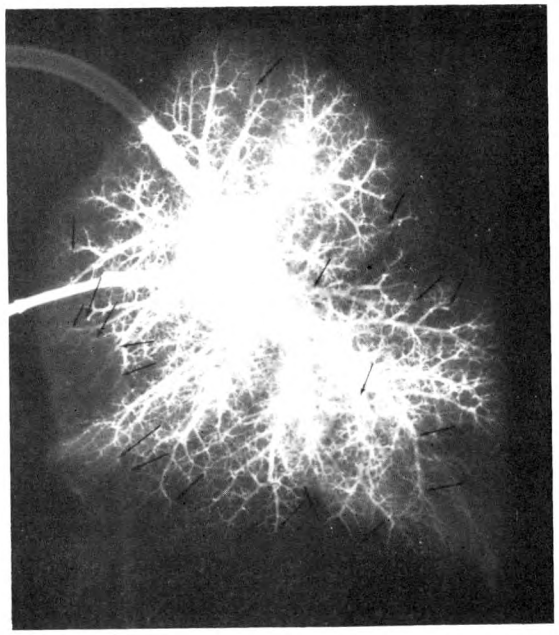


FIG. 11. Postmortem pulmonary arteriogram in human with microembolism (arrows indicate sites of emboli)—periphery of lung is ischemic.

we have described? On a Gough section of a lung, one may diagrammatically represent peripheral ischemia similar to that which can be observed in autopsy material or produced experimentally in animals (Fig. 13). If radioactivity on pulmonary scintigrams were confined to the area within the line, each lobe would appear reduced in volume and a zone of decreased radioactivity in the perifissural area would be seen. Decreased activity along the fissure will be apparent on the scintigram because it is contrasted with relatively normal activity in the adjacent central portions of each lobe. Conversely, decreased activity around the outer periphery of each lobe may not be apparent because there is nothing with which to contrast it. It bears emphasis that scintigrams do not necessarily show the outer border of the lung, but rather only the outer margin of radioactivity in the lung. Accordingly, the "shrunken lobe" is less often observed than is "fissural visualization."

Apart from the purely mechanical effects of multiple pulmonary microemboli, two additional phenomena which accompany this condition could contribute to the scintigraphic patterns we have described. First, reflex vasoconstriction has been demonstrated to occur in the small peripheral pulmonary arteries subsequent to arteriolar embolism.[3,14] There is no direct evidence bearing on this point, but such vasoconstriction might be expected to decrease the amount of radioactivity reaching the periphery of the lungs—at least in the acute period after embolism. Secondly, as documented earlier (Fig. 12), development of bronchopulmonary collateral circulation after pulmonary embolism sometimes occurs. In the living patient, blood flow will occur from the bronchial arteries into the pulmonary circulation creating a potentially significant effect on lung scintigrams (Fig. 14). After intravenous injection, radioactivity reaches the lungs only via the pulmonary arteries. Nearly all the particles are filtered in the pulmonary capillary

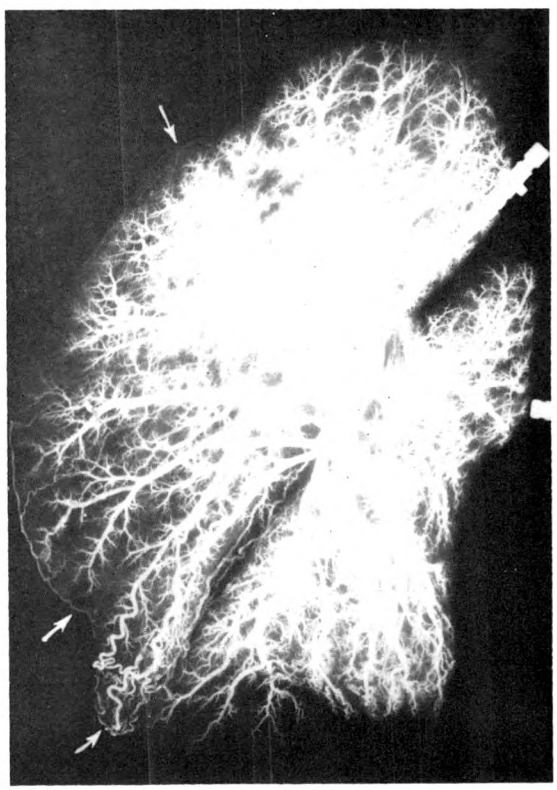


FIG. 12. Postmortem pulmonary arteriogram in human with microembolism—arrows indicate bronchial collaterals which have developed around periphery of upper lobe.

bed so that systemic blood is free from radioactivity. This includes blood carried by the bronchial arteries. Accordingly, portions of lung supplied by bronchial collateral circulation will be essentially nonradioactive. Since bronchial collaterals develop around the periphery of the lung, a peripheral zone of decreased radioactivity will result (Fig. 14).

Multiple pulmonary microembolism is the most common form found in carefully studied autopsy material.[11] Several mechanisms have been postulated for such microembolism. Multiple small emboli may be discharged in showers or sequentially from larger thrombi in the extremities or pelvic veins. Alternatively, large emboli formed peripherally may fragment during their passage through the heart.[13] In both

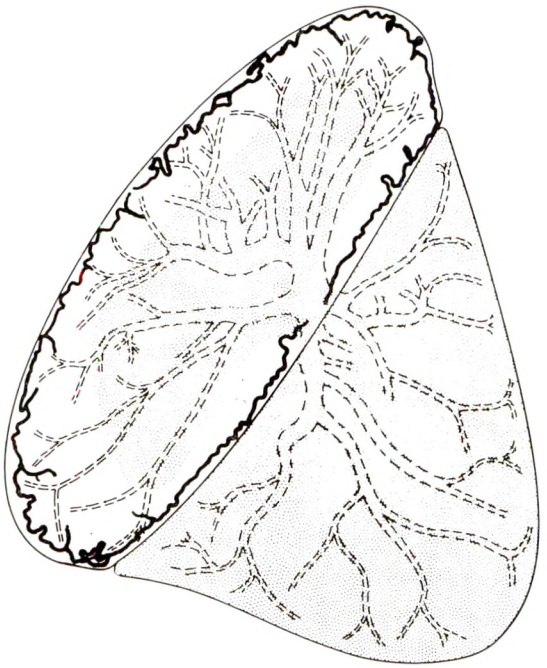


Fig. 14. Bronchial collateral flow supplies nonradioactive blood to the periphery of the upper lobe. A "shrunken" upper lobe and "fissural visualization" might be the scintigraphic result.

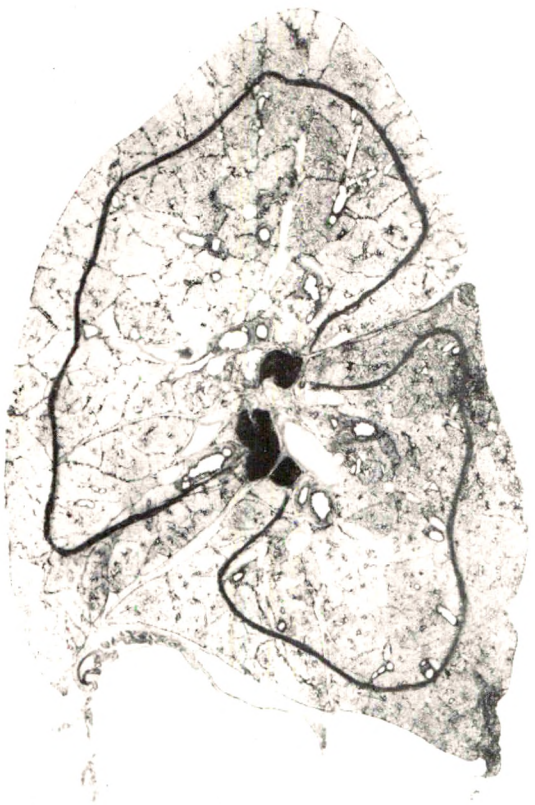


Fig. 13. Gough section of human lung on which peripheral ischemia has been diagrammatically represented. (Reproduced with permission from *The American Journal of Cardiology*.)

of these situations, small emboli would be distributed to all regions of the lungs in a fairly random fashion. Finally, large emboli initially arrested in central pulmonary arterial branches may disintegrate and the resulting microembolic fragments will then be distributed to the more peripheral vessels in the involved lobe or segment.

SUMMARY

A two fold scintigraphic pattern consisting of (1) decreased radioactivity along the interlobar fissure and (2) apparent diminution in the size of involved lobes is presented. The findings appear to result from multiple pulmonary microembolism—a disease entity which occurs commonly and which can produce a circumferential zone of pulmonary hypoperfusion. Reflex peripheral vasoconstriction and development of bronchopulmonary collaterals may augment this effect.

"Fissural visualization" is seen more often than the "shrunken lobe," but both

are fairly frequent findings. To the authors' knowledge, neither has been previously reported. It is hoped that recognition of these patterns will aid in the detection of multiple pulmonary microembolisms in the future.

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INTRAVAGINAL MARKERS FOR ACCURATE RADIONUCLIDE LOCALIZATION OF THE PLACENTA*

By LEONARD ROSENTHALL, M.D.†
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IMAGING of the placenta with radiopharmaceuticals[1–5] has been shown to be more definitive than the older surface spot counting technique.[4] The usual manner of defining the location of the placenta by the former method was by placing a radioactive marker over the symphysis pubis and measuring the distance between the leading edge of the placenta and the marker. It was assumed that the marker reflected the level of the cervical os. Much to our consternation, 2 patients presented with placentas which measured 6 and 6.5 cm., respectively, above the symphysis pubis marker and were read as "low-lying," when in fact they were previa. This prompted an investigation of the use of intravaginal radionuclide markers as a means of locating the cervix on the scan.

METHOD AND MATERIAL

The placentas were visualized with either radiopertechnetate,[1,3,4] technetium 99m labeled human serum albumin,[2] or acid indium 113m.[5] About 1 to 2 mc of the radiopharmaceutical was injected intravenously, and the gamma-ray scintillation camera was set to accumulate 100,000 counts for each of the frontal and lateral projections.

The symphysis pubis marker consisted of a point source of high specific activity I^{131} or Au^{198}. This was accomplished by drawing up 1/20 ml. of the radionuclide into a one-half milliliter disposable syringe, which was then taped to the pubis (Fig. 1). In order to secure an intravaginal point source which could be easily directed into the posterior fornix with a minimum of trauma, a long semi-flexible teflon tube was employed. The lumen at the end of the tube was sealed with cotton batting. One-tenth of a milliliter of high specific activity I^{131} or Au^{198} was deposited at the bottom of a pro-

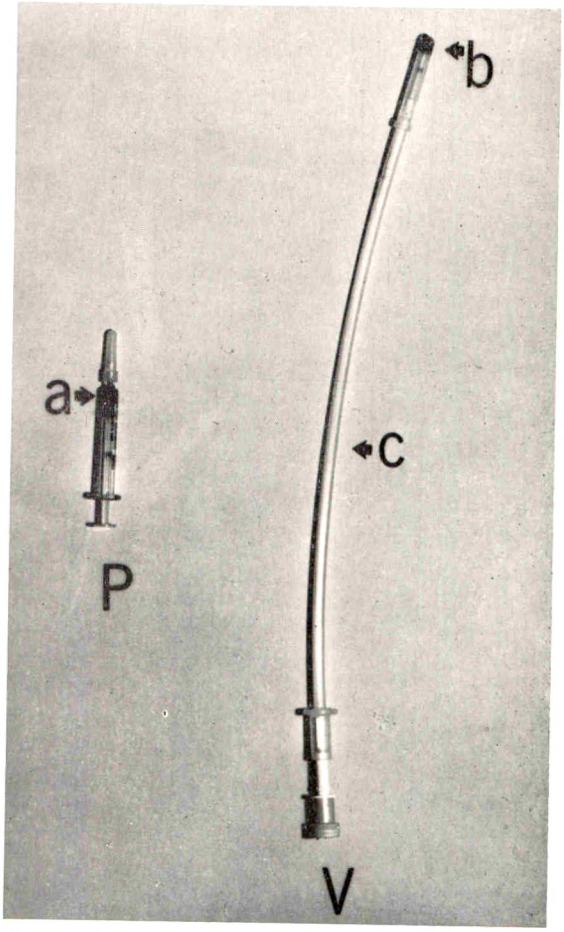


FIG. 1. Radionuclide markers used in this study. P = symphysis pubis marker; a = ½ ml. syringe containing 1/20 ml. high specific activity I^{131} or Au^{198}; V = intravaginal marker; b = protective cap from a disposable needle containing 1/10 ml. high specific activity I^{131} or Au^{198}. It is fixed onto c; c = the Abbott disposable cervical-pudendal injection set.

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TABLE I

MEASUREMENTS OF DISTANCE

Case No.	Gestation (wk.)	Lateral View "a" (cm.)*	Frontal View "b" (cm.)†
1	40	13.5	4.5
2	40	10.0	8.0
3	32	11.5	4.5
4	32	11.5	6.0
5	32	10.0	2.5
6	32	12.0	2.5
7	32	14.0	7.0
8	32	7.5	4.0
9	32	10.0	4.0
10	28	8.5	4.0
11	28	9.0	0.0
12	26	11.5	4.5
13	24	13.0	4.5
14	24	8.0	0.0
15	24	12.5	3.0
Average		11.0	4.0
Range		7.5–14	0 to 8

* a = the perpendicular distance in centimeters between the symphysis pubis marker (P) and the horizontal line passing through the intravaginal marker (V), in the lateral projection.

† b = the distance in centimeters between the symphysis pubis marker (P) and the intravaginal marker (V), in the frontal projection.

tective cap from a disposable needle and then fixed to the sealed end of the teflon tube. An air-lock between the sealed end of the tube and the radioactive material prevents the latter from flowing away from the tip. The Abbott disposable cervical-pudendal injection set* is most easily adapted to these constraints (Fig. 1).

Insertion of the intravaginal marker was procured blindly by gentle posterior and forward advancement until it could proceed no further, or, alternatively, a speculum was used for visual placement in the posterior fornix.

Fifteen pregnant females were used in this study. Gestation varied from 24 to 40 weeks. All were premedicated with 250 mg. potassium perchlorate when radiopertechnetate or technetium 99m labeled human serum albumin was employed as the test agent. There is no safe premedication for acid indium 113m; however, there is no specific organ deposition of the radionuclide and a 1 mc dose yields a total body absorbed dose of about 12 rads, which is acceptable.

RESULTS

Table 1 contains the measurements of the distances between the symphysis pubis marker (P) and the intravaginal marker (V) in the frontal and lateral projections. The measurement "a" is the perpendicular distance in centimeters between P and the horizontal line passing through V in the lateral projection (Fig. 2*A*). In the frontal projection, "b" denotes the distance in centimeters between P and V (Fig. 2*B*). An

* The Abbott Laboratories, North Chicago, Illinois.

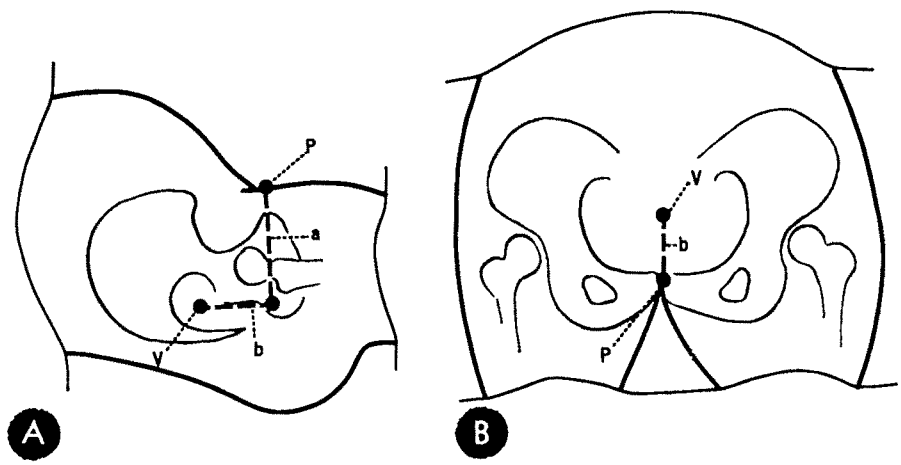


FIG. 2. Schematic drawing of lateral (*A*) and frontal (*B*) views of the pelvis. P = radionuclide marker on the symphysis pubis; V = radionuclide marker in the posterior vaginal fornix; a = the distance between P and a horizontal line passing through V; b = the distance between P and V in the frontal projection.



FIG. 3. Right lateral acid indium 113m scan of a patient near term, showing the symphysis pubis marker P and intravaginal marker V in relation to the placenta, which is implanted on the posterior wall of the uterus. The placenta could not be visualized in the frontal projection as it presented as a diffuse background.

average value of 4.0 cm. was obtained for "b," with a range of 0 to 8 cm. The average for "a" was 11 cm., with a range of 7.5 to 14 cm.

Figure 3 is an illustration of a posterior wall implantation of a placenta in the lateral projection with the markers in place.

DISCUSSION

It is apparent from our results that on the average the posterior fornix of the vagina lies about 4 cm. cephalad to the symphysis pubis. More importantly, it can be as much as 8 cm., and this would tend to lessen the value of the symphysis pubis marker as a reference point. A low-lying placenta can be delivered through the vagina, whereas a placenta previa necessitates a cesarean section, and reliance on the pubic marker may mislead the obstetrician into a vaginal delivery. Figure 4, *A* and *B* is a case in point. There was a persistent transverse lie and occasional spotting. At 36 weeks gestation a radiopertechnetate placental scan was obtained, and it was read as low-lying because the distance of the inferior edge of the placenta and the symphysis pubis marker in the frontal view was 6.5 cm. Despite the radionuclide study, the obstetrician proceeded with a cesarean delivery and a placenta previa was encountered. Another case, published elsewhere,[4] was miscalled as low-lying because the distance between the organ and the symphysis pubis was 6 cm. In both these patients error could have been avoided with an intravaginal marker.

Our obstetricians have no qualms about the placement of the intravaginal marker. The gentle mode of insertion and the slender diameter of the tubing will cause little disturbance. Alternatively, a speculum can be employed and the tip of the marker eased into place under direct observation.

It was observed in this study that the P-V distance in the frontal projection was greater in those patients closer to term. Two of the patients with P-V measurements of 7 and 8 cm., respectively, had fetuses in persistent transverse lie.

SUMMARY

Fifteen pregnant patients were studied with regard to the accuracy of the symphysis pubis as an indirect indicator of the position of the internal cervical os in placental imaging. A radionuclide marker was placed in the posterior vaginal fornix to

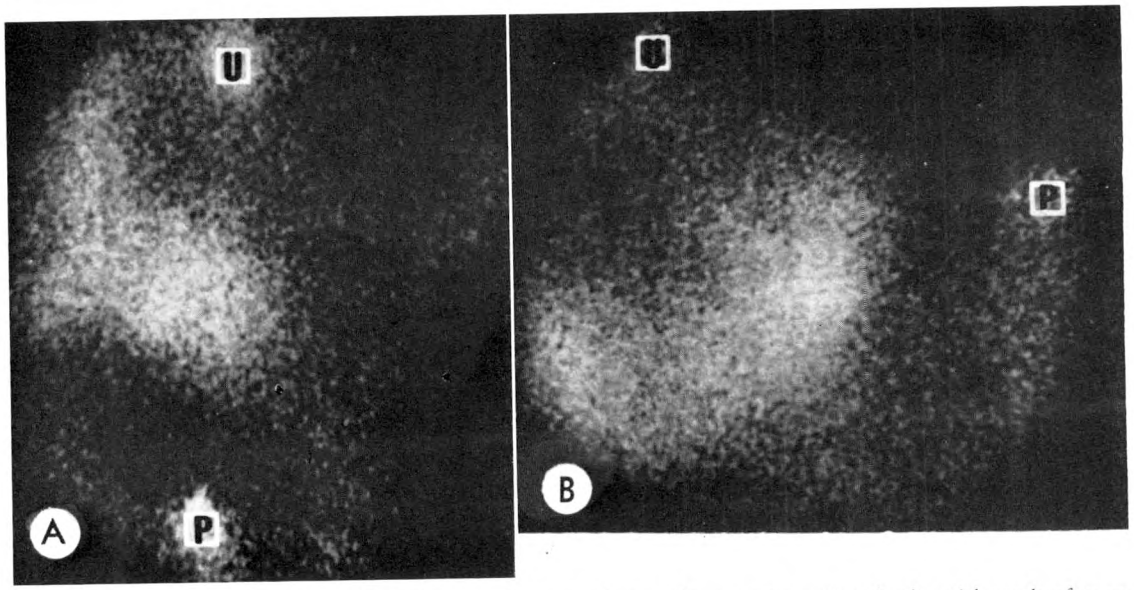


FIG. 4. Frontal (*A*) and lateral (*B*) radiopertechnetate placental scans of a patient in the 36th week of pregnancy. The distance between the symphysis pubis marker P and the inferior edge of the placenta measures 6.5 cm. This was originally miscalled a "low-lying" placenta, when in fact it was a placenta previa. U = umbilicus.

approximate the region of the internal cervical os. The distance between this marker and the one placed over the symphysis pubis ranged from 0 to 8 cm., with an average of 4 cm. It is concluded that an intravaginal, rather than a pubic, marker is required to distinguish placentas which are low-lying and previa, since the two conditions necessitate divergent management. This is particularly true of those patients wherein the fetus is in a transverse lie and the cervix is pulled cephalad.

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SIMPLIFICATION OF DETERMINATION OF SERUM THYROXINE IODINE BY COMPETITIVE BINDING ANALYSIS*

By MARTIN L. NUSYNOWITZ, LTC, MC, USA, *and* JEROME WALISZEWSKI
EL PASO, TEXAS

THE search for methods more specific than the protein bound iodine test for the determination of serum thyroxine and thyroxine iodine concentration has led to the development of the assay of this hormone by the principle of competitive binding analysis.[2,4,5,6] This assay is based on the comparison of the quantity of tracer radiothyroxine displaced from thyroxine binding globulin (TBG) by the addition of known amounts of l-thyroxine with the quantity displaced by an extract of serum. The purpose of this communication is to: (1) describe several modifications which improve the procedure; (2) report the results obtained in normal young men of the concentration of serum thyroxine iodine by competitive binding (T_4CBI); (3) compare these values with simultaneously determined protein bound iodine (PBI) and thyroxine iodine by column chromatography (COL T_4I); and (4) show the range of results in various clinical conditions.

MATERIAL AND METHODS

The commercially available Tetrasorb* I^{125} T_4 diagnostic kit was employed for the determination of serum thyroxine and thyroxine iodine by competitive binding analysis. This kit utilizes a resin impregnated sponge as a secondary binding site for displaced unbound radiothyroxine to separate it from tracer bound to TBG. We have followed the method described in the product literature except for the following modifications:

(1) *Preparation of Standards and Determination of Extraction Efficiency.* Duplicate thyroxine working standards, prepared with each lot of samples processed, are made in artificial serum consisting of 4.5 gm. of salt-poor human serum albumin and 2.5 gm. of gamma globulin in 100 ml. of water. The addition of 0, 10, 20, 30, and 40 μl. of a stock solution containing 5 μg. l-thyroxine per ml. to tubes containing 1 ml. of artificial serum produces working standards of 0, 5, 10, 15 and 20 μg. thyroxine per 100 ml. "serum," respectively. Following mixing, the working standards are incubated at room temperature for 1 hour and then extracted simultaneously with the lot of unknown samples processed. Hence, any factor affecting the extraction of the unknowns equally affects the extraction of the standards.

(2) *Sample Counting.* Since careful and accurate pipetting will ensure that equal amounts of radiothyroxine are added to each sample, the first of the 2 counts performed on each sample can be totally eliminated, as has been described for the T-3 resin sponge uptake test.[8] After washing removes the TBG-bound radiothyroxine from tracer bound to resin, samples are counted by the preset time method for a period which ensures good counting statistics for the sample containing the smallest quantity of tracer (0 μg. per 100 ml. standard).

Results are reported as thyroxine iodine by competitive binding (T_4CBI) by multiplying the concentration of serum thyroxine by 0.653 in order to facilitate comparison with other measures of hormonal concentration. Protein bound iodine was

* Abbott Laboratories.

* From the Radioisotope-Endocrine and Research and Development Services, William Beaumont General Hospital, El Paso, Texas. This material has been reviewed by the office of The Surgeon General, Department of the Army, and there is no objection to its presentation and/or publication. This review does not imply any indorsement of the opinions advanced or any recommendation of such products as may be named.

TABLE I

SERUM THYROXINE IODINE BY COMPETITIVE BINDING, BY COLUMN, AND PROTEIN BOUND IODINE ON SERA OF 40 NORMAL YOUNG MEN (μg./100 ml.)

	T_4CBI	COL T_4I	PBI
Mean	5.6	4.9	5.8
Population standard deviation	0.9	0.6	1.1
Standard error	0.1	0.1	0.2
Minimum	4.0	3.9	4.0
Maximum	7.2	6.3	8.4
Skewness	−0.1	+0.1	+0.1
Kurtosis	2.2	2.5	2.4

T_4CBI = thyroxine iodine by competitive binding.
COL T_4I = column chromatography.
PBI = protein bound iodine.

measured by the method of Riley and Gochman,[10] while COL T_4I determinations were performed by the Bio-Science Laboratories, Van Nuys, California.[9]

RESULTS

Table I reveals the results obtained for the T_4CBI, COL T_4I, and PBI on 40 normal young men. Identical results were obtained for the T_4CBI when standards made as recommended by the product literature were used and the values obtained were corrected by separate determination of extraction efficiency. The normal range (95 per cent confidence limits) of T_4CBI, as determined from this sample of 40 normal young men is 3.8 to 7.4 μg. per 100 ml. Table II shows the relationships between the 3 tests. There is no significant difference between the values obtained for the PBI and the T_4CBI, although the former tends to run slightly higher. Both the PBI and the T_4CBI show small but significant differences when compared with the COL T_4I. The T_4CBI results in a variety of clinical settings are shown in Table III.

TABLE II

RELATIONSHIPS AMONG SERUM THYROXINE IODINE BY COMPETITIVE BINDING, BY COLUMN, AND PROTEIN BOUND IODINE

	T_4CBI-COL T_4I	PBI-T_4CBI	PBI-COL T_4I
Mean difference	0.7	0.2	0.9
Standard deviation	0.6	1.1	1.1
Standard error	0.1	0.2	0.2
Maximum difference	2.4	2.5	3.2
t	7.	1.0	4.5
P	<.001	N.S.	<.001
Correlation coefficient	0.66	0.42	0.41

DISCUSSION

The currently recommended method for the performance of this test employs a series of thyroxine standards which are added directly to the TBG-tracer solution, while dried alcohol extracts of sera are processed in a similar fashion. In order to obtain truly meaningful results, each laboratory must separately determine extraction efficiency for each batch of solvents, and it is assumed that other factors influencing extraction efficiency when sera are being processed are sufficiently constant so that they may be neglected. With the modification proposed herein, any factor affecting extraction of the unknown sera will equally affect the extraction of the standard solutions, and the separate determination of extraction efficiency becomes totally unnecessary. We have found that no significant amount of thyroxine is present in the artificial serum, and the results obtained are practically identical to those obtained using currently recommended methods.

Ekins, in a discussion of Murphy's

TABLE III

T_4CBI (μg./100 ml.) IN VARIOUS CLINICAL STATES

Condition	No.	Range	Mean
Euthyroid women on estrogens	12	8.1–12.9	10.8
Overt thyrotoxicosis	13	>13	
Overt hypothyroidism (various causes)	13	0.3–2.2	1.5
Familial thyroxine binding globulin deficiency	1	2.0	
Severe hypoproteinemia	1	2.0	

paper,[2] recommended that correction for extraction, a practice not uniformly employed, be performed routinely in order to facilitate intercomparisons among different laboratories. In addition, we feel that the results should be reported as thyroxine iodine rather than thyroxine in order to facilitate comparison among different tests.

The one-step counting modification enables one technician to process upwards of 100 samples per day conveniently. The limiting step is the time required for drying the ethanol extracts of serum. Freeze drying the extract, if lyophilization equipment is available, will considerably shorten this time without affecting the results.

These modifications, while simplifying the procedure considerably, give results that are almost identical to the reported values.[3,6,7] The similarity in the absolute values obtained for the T_4CBI and the PBI (Table II) makes direct intercomparison between the methods possible. In only 1 of the 40 individuals did the PBI exceed the T_4CBI by more than 2 μg. per 100 ml. The use of both of these tests simultaneously would serve as a useful gauge of the concentration of nonhormonal protein bound iodine liberated into the circulation by the thyroid gland, as in thyroiditis.

The superb specificity and diagnostic usefulness of the serum thyroxine iodine by competitive binding analysis is now well documented;[1,6,7] the results we obtained suggest that the modifications described in this paper simplify this test with no sacrifice in diagnostic accuracy.

SUMMARY

The method for the serum thyroxine iodine by competitive binding analysis (T_4CBI) has been greatly simplified.

The results are identical to those obtained by using standard methods; correlation with thyroxine iodine by column chromatography is high, and there is no significant difference when compared to protein bound iodine in normals.

The T_4CBI values in a variety of clinical conditions are as expected.

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MARROW CELL INJURY FOLLOWING Ca^{45} UPTAKE IN BONE: CHANGES IN MARROW AND PERIPHERAL BLOOD CELLULARITY*

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A NUMBER of studies inquiring into the nature of calcium metabolism and its relationship to bone metabolism have been reported in the last few years.[2-4] The use of radioisotopes as tracers in these studies and in diagnostic procedures has been increasing steadily, although evidence has only recently been forthcoming on the effects of radiation from these isotope sources on surrounding tissue.[1]

The International Commission of Radiological Protection has fixed the maximum permissible body burden of Ca^{45} at 30 μc for total body as of 1964.[12] It is possible, however, that a dose within the range specified as permissible for total body burden, would result in a biologically significant fixed bone pool due to the nature of calcium metabolism in bone. In addition, since Ca^{45} is closely approximated to marrow when initially absorbed and it emits a 250 kev. beta particle, effects on marrow cells from doses within the permissible limits for bone and body burden are to be expected and indeed have been observed and reported.[1] Radiation effects were demonstrated in rats after treatments with increasing doses of Ca^{45} from 25 μc to 300 μc. Even after 25 μc, micronuclei were observed to increase six-fold in 24 hours and the mitotic index was significantly reduced in all treatment groups.

Because radiation effects were demonstrated at all Ca^{45} treatment levels, the 25 μc and 100 μc Ca^{45} doses were chosen as being representative treatments, and the original experiments were expanded to include effects on the marrow cellularity.

The purpose of this paper is, therefore, to show that continuous low level radiation delivered to the marrow from radioactive calcium deposited in bone, causes changes in the cellularity in the marrow and blood that are as extensive as when higher doses of x rays or gamma rays are used. In addition, evidence is presented to indicate that inhibition of reproductive capacity as well as cell destruction and accelerated cell removal, play a part in the depletion of the marrow.

MATERIAL AND METHODS

Eighty albino male, Sprague-Dawley rats, 3 months old and weighing 300 ± 20 grams, were grouped and treated with Ca^{45} (dissolved in 0.5 *N* HCl) injected intraperitoneally. One experimental group received 25 μc of Ca^{45}, one group received 100 μc of Ca^{45}, and the other served as controls. All animals were fed a standard laboratory ration and drinking water.

Marrow samples were taken at 1, 2, 4, 6, 7, 12, 14, 30 days, and 5 months following isotope injection. Both tibiae from each animal were sliced longitudinally and samples of marrow were diluted 1/1,000 in 0.1 *N* HCl. The number of nucleated bone marrow cells per $mm.^3$ was determined on a hemocytometer. Other marrow samples were removed with a small forceps, prepared as a squash, dehydrated with methyl alcohol and air dried. The cells were subsequently stained with Wright's stain and a differential count made. At least 400 cells from each slide were counted and the absolute number of myeloid, erythroid and lymphocyte cells present was calculated by multiplying the fraction of each cell type in the differential by the total number of nucleated marrow cells/$mm.^3$ at each time

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sample. All other cells present, including damaged forms, were included in the differential count. The resulting data from these marrow differentials were divided into 4 groups for presentation in this paper: (1) All of the dividing and differentiating nucleated erythroid cells of the marrow; (2) the dividing and differentiating myeloblasts, myelocytes, and metamyelocytes; (3) the juvenile granulocytes or bands which are found both in the marrow and in the peripheral blood of normal rats; and (4) the mature granulocytes found both in the peripheral blood and in large numbers in the marrow as the mature granulocyte pool.

A sample of peripheral blood was obtained from the tail vein of each animal before it was sacrificed. Staining was effected by mixing equal drops of blood and new methylene blue (0.5 per cent) in a test tube for 10 minutes. Smears were made and air dried. All data concerning changes in the peripheral blood are reported as per cent. One thousand red blood cells from each animal were counted to determine the reticulocytes present in the peripheral blood. These smears were then counterstained with Wright's stain and a white cell differential count made. The percentages of mature and immature granulocytes in the blood are reported.

The radiation doses received by the animals from β decay of Ca^{45} were calculated using the following equation:

$$D_\beta = 73.8\overline{E}_\beta C_0 T_E(1 - e^{-0.693t T_E}) \text{ rads},$$

where $D_\beta = \beta$ dose in rads; $\overline{E}_\beta =$ average β energy in mev.; $C_0 =$ microcuries of isotope/gram of bone tissue; $T_E =$ effective half-life of Ca^{45}; and $t =$ time elapsed since injection.

Two values for C_0 were used in the above equation: (1) rat body weight and (2) rat skeletal weight, the latter giving an approximate dose to the marrow.

The calculated radiation doses from 25 μc and 100 μc of Ca^{45} at various sample times after injection appear in Table 1. There is initially a very rapid rate of uptake of available Ca^{45} by bone.[2] However, according to Harrison *et. al.*,[4] 30 to 50 per cent of the initial calcium accretion returns to the extracellular fluid and is excreted within 2 to 4 days. The remainder is excreted only very slowly and represents calcium in a relatively fixed bone pool. The effective half-life of Ca^{45} for the fixed bone pool is estimated as 162 days. Some of the calcium from the bone, even though relatively fixed, is from time to time alternately resorbed and accreted, thus introducing another unknown factor as to the availability of Ca^{45} at any one time for irradiation of the marrow. The calculations of dose using this equation, therefore, is at best only a rough estimate. The true total dose is assumed to fall within the range indicated in Table 1 to whole body and to marrow.

TABLE I

CALCULATED RADIATION DOSES AT VARIOUS TIMES AFTER Ca^{45} INJECTION

Sample Time after Injection of Ca^{45} (days)	Radiation Dose from 25 μc of Ca^{45} (rads)		Radiation Dose from 100 μc of Ca^{45} (rads)	
	to whole body	to marrow	to whole body	to marrow
1	1.28	11	5.14	43
2	2.41	21	10.28	86
4	5.37	43	20.44	172
6	7.60	64	30.49	255
7	8.55	75	34.31	297
12	14.90	126	60.14	503
14	17.28	146	69.82	584
32	38.44	322	154.23	1290
150	>150	>1250	>600	>5000

RESULTS

A. Ca^{45} EFFECTS ON THE CELLULARITY OF THE MARROW

The first change noted in the marrow cellularity as the result of Ca^{45} deposition in the bone, was the sudden drop in the number of nucleated marrow cells. The number of nucleated cells in the 100 μc group, fell to a point that was 25 per cent below control values within the first day of receiving Ca^{45} (Fig. 1). The calculated radiation dose

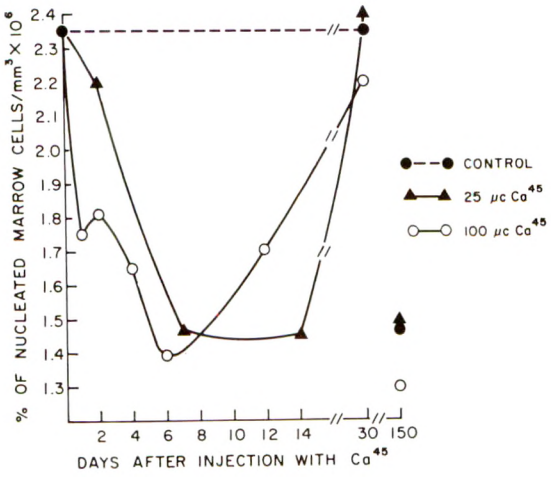


FIG. 1. Changes in the total number of nucleated marrow cells after deposition of Ca^{45} in the bone.

to the marrow on Day 1 was 43 rads and on Day 2 was 86 rads (refer to Table 1 for doses at other times). By the 6th day, the number of nucleated cells had decreased to a level 42 per cent below normal and was still 30 per cent less than the control value at the end of 2 weeks. When sampled at 30 days, the count had risen to a point which was about 7 per cent below normal and was still 10 per cent below the normal figure at 5 months. The control values were lower at 5 months than at the beginning of the experiment due to a normal decrease in marrow activity in the long bones associated with the increasing age of the animals (Fig. 1).

The 25 μc treatment group, also exhibited a decrease in the number of nucleated marrow cells although not as rapid as seen in the animals treated with 100 μc and it was only slightly below the control values 2 days after receiving Ca^{45} (Fig. 1). By the 7th day, however, the cell number was 40 per cent below normal and remained that low through the 2nd week. The calculated radiation dose at 7 days in the 25 μc group was 75 rads. The 30th day marrow samples showed a return to normal numbers. At 5 months, the number of nucleated marrow cells was the same as in controls.

B. VARIATIONS WITHIN THE MYELOID ELEMENT OF THE MARROW AND PERIPHERAL BLOOD RESULTING FROM CA^{45} DEPOSITION IN BONE

(1) *Myeloblasts, myelocytes, and metamyelocytes.* The number of myeloblasts, myelocytes, and metamyelocytes decreased slightly at Day 1 after the 100 μc treatment with Ca^{45} (Fig. 2*A*). It then increased to 1.2 times the control value on Day 2. The number of cells began a decline between

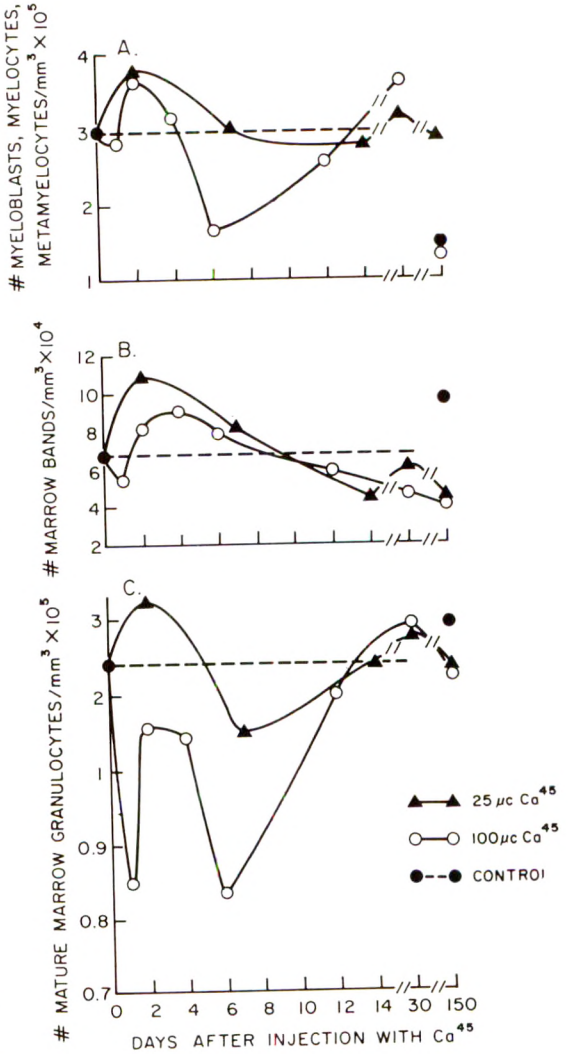


FIG. 2. (*A-C*) Variations in numbers of myeloid cells in the marrow after deposition of Ca^{45} in bone. (*A*) Myeloblasts, myelocytes and metamyelocytes. (*B*) Marrow bands. (*C*) Mature marrow granulocytes.

Days 2 and 3, and reached a minimum on Day 6 which is 50 per cent below normal (calculated dose 255 rads). On Day 12 the number of myeloblasts, myelocytes and metamyelocytes was 16 per cent below controls. At 30 days the number had risen to about 1.2 times the control values and at 5 months the values appeared normal.

Also in Figure 2*A* are the data from the 25 μc treatment group. The number of myeloblasts, myelocytes, and metamyelocytes rose to 1.3 times the normal number by Day 2. Sampling through the following 30 days revealed the values to be very near those for controls, but peculiarly enough at 5 months were twice the normal number.

(2) *Marrow bands.* There was a 20 per cent decrease in marrow bands by Day 1 in animals receiving 100 μc of Ca^{45} (43 rads). Figure 2*B* shows that after this initial decline in marrow bands the number increased to about 1.3 times above normal on Days 2, 4 and 6. By the end of 2 weeks the number of marrow bands was again about 15 per cent below normal and at 30 days 40 per cent below control values.

In animals receiving 25 μc of Ca^{45} the number of marrow bands was 1.6 times above normal on Day 2, and 1.2 times above at the end of the first week. At 2 weeks the number had fallen to 40 per cent below control values and at 30 days was only slightly less than normal.

Five months later the values for marrow bands in both the 25 μc and 100 μc Ca^{45} treatments were about 50 per cent below the normal (Fig. 2*B*).

(3) *Mature marrow granulocytes.* The changes in the numbers of mature cells in the marrow granulocyte pool can be seen in Figure 2*C*. There was a 65 per cent decrease in the number of cells in this pool within 24 hours of receiving 100 μc of Ca^{45} (43 rads). A rebound toward control values occurred on Days 2 and 4 but the number was still 35 per cent below normal. Another drop to about 65 per cent below control values occurred by Day 6 before the number of mature marrow granulocytes increased to a point 15 per cent below normal at Day 12 (calculated dose 503 rads). At the end of 30 days the value was about 10 per cent above controls.

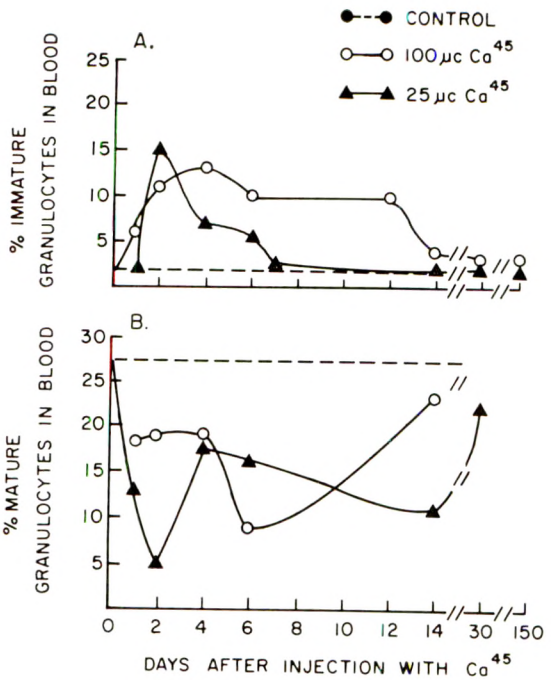


FIG. 3. (*A* and *B*) Variations in percentages of mature and immature granulocytes in peripheral blood after Ca^{45} deposition in bone.

In the 25 μc group (Fig. 2*C*) the number of mature granulocytes increased by Day 2 to 1.4 times above control values, then fell to a point 35 per cent below normal at the end of the first week (calculated dose 75 rads), but at 2 weeks the number was back to normal and at 30 days was slightly above.

At 5 months the number of mature marrow granulocytes in both treatment groups was 15 per cent below the control average.

(4) *Immature granulocytes in the peripheral blood.* That there was an effect on the peripheral blood picture, as the result of changes produced in the bone marrow by deposition of Ca^{45} in the bone, can be readily seen in Figure 3*A*, which shows a large and rapid increase in the percentage of the immature granulocytes in peripheral blood. In the 100 μc group, the immature

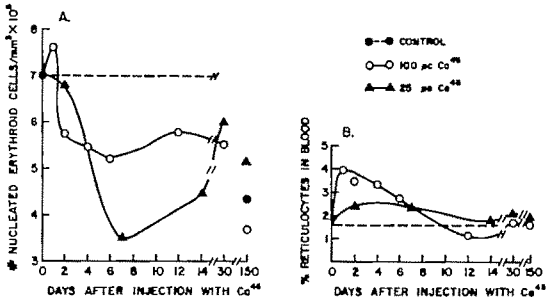


FIG. 4. (*A* and *B*) Variations in the erythroid cells of the marrow and of the reticulocytes in blood after Ca^{45} deposition in bone.

granulocytes increased to 3 times the control value at Day 1, 6 times the control at Day 2, and was at a point 7 times the control values by Day 4 after Ca^{45} injection. The number fell slightly by Day 6 to 5 times normal, and was still the same by the 12th day. At 30 days and at 5 months, the number of immature granulocytes in the peripheral blood was normal.

The 25 μc Ca^{45} treatment resulted in counts of immature granulocytes which were normal at Day 1 after injection of Ca^{45} but increased sharply to 7 times normal by Day 2 (calculated dose 21 rads). The counts fell to a point that was still about 3 times higher than the control averages by Days 4 and 6, and were normal again at 7 days, 14 days, 30 days, and at the 5 month sampling times. These results are presented graphically in Figure 3*A*.

(5) *Mature granulocytes in the peripheral blood.* It can be seen in Figure 3*B* that the percentage of mature granulocytes in the blood of animals given 25 μc of Ca^{45} falls to a much lower value by Day 2 than it does in animals receiving 100 μc of Ca^{45}. In the 25 μc group the mature granulocytes of the blood are decreased by 50 per cent by Day 1 and drop to 82 per cent below control values on sample Day 2. By the 4th day, some of this depletion in numbers had been recovered but the count was still 37 per cent below normal, as it was on Day 6. Two weeks later the per cent mature granulocytes had again decreased to only 65 per cent of the control averages and was still 15 per cent less than normal at 30 days, although the number appeared to be increasing toward normal.

The 100 μc treatment resulted in a granulocyte count 33 per cent below controls in the first 24 hours and remained from 30 to 33 per cent below normal through Day 4 (Fig. 3*B*). By Day 6, the count had fallen again to a point 67 per cent below normal, increased to 15 per cent below normal at 2 weeks and was the same as control averages at 30 days.

C. VARIATIONS IN THE ERYTHROID ELEMENT OF THE MARROW AND PERIPHERAL BLOOD RESULTING FROM CA^{45} DEPOSITION IN THE BONE

(1) *Marrow erythroid cells.* The number of erythroid cells was 1.1 times the normal in the first 24 hours after injections of 100 μc of Ca^{45} (Fig. 4*A*). This was followed by a steep decline in cell number reaching a level of 20 per cent below controls by Day 2 (calculated dose 86 rads). The number remained from 25 to 30 per cent below normal through Day 30. The number of cells in the 25 μc treatment fell only slightly by Day 2, but reached a point that was 50 per cent below control values and, remarkably, 25 per cent lower than the values obtained for the 100 μc group by the end of the first week after Ca^{45} injection and 2 weeks later was still 35 per cent below normal. The cell number then began to increase but was still 20 per cent less than the value for the average control animal at 30 days.

At 5 months the number of erythroid cells in the 25 μc group was 20 per cent above control values and the number in the 100 μc group was about 20 per cent below the control value (Fig. 4*A*).

(2) *Reticulocytes in the peripheral blood.* Figure 4*B* demonstrates the rapid rate of increase in peripheral blood reticulocytes in animals receiving 100 μc Ca^{45}. By 24 hours, the number of reticulocytes was 2.5 times higher than controls. The count declined gradually to 2.1 times normal at Day 4, 1.8 times normal at Day 6, and by Day 14 after the Ca^{45} injection was actually slightly

below normal. Samples taken at 30 days and at 5 months appeared normal.

Animals receiving 25 μc of Ca^{45} had a reticulocyte count that did not increase as fast as the group treated with 100 μc but was still 1.5 times higher than the controls at Day 2 and Day 7, although at 14 days, 30 days, and 5 months, the counts appeared normal.

D. Effects of Ca^{45} on mitosis in the cells of the bone marrow

(1) *Percentage of dividing myeloid cells.* Control animals had an average of about 1.5 per cent of the myeloid cells undergoing mitosis (Fig. 5*A*). Within 24 hours of receiving 100 μc Ca^{45} mitosis had dropped to 0.66 the control value. By Day 2, the number of mitotic cells was 1.7 times as high as the controls, but was only 0.5 times as much as normal on the 4th day and again 2 times the control on Day 6. At the end of the 2nd week, the number of myeloid cells dividing was still about 60 per cent below normal. Samples at 30 days and 5 months revealed that the per cent mitosis was still below normal.

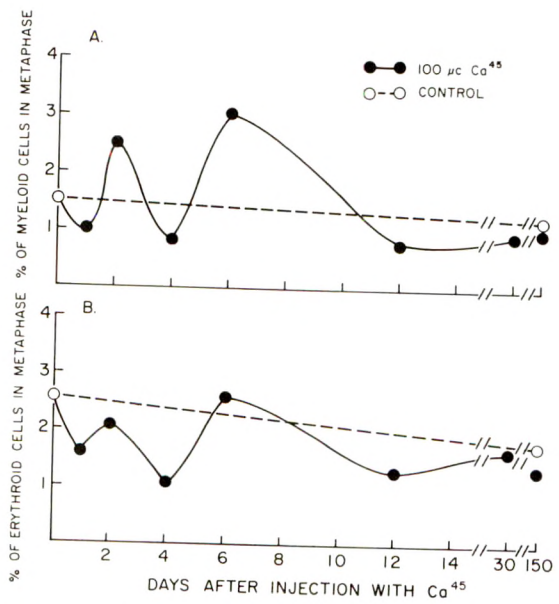


Fig. 5. (*A* and *B*) Effects on the per cent of the myeloid and the per cent of the erythroid cells dividing after deposition of Ca^{45} in bone.

(2) *Percentage of dividing erythroid cells.* Figure 5*B* shows the effect of Ca^{45} on cell division in the erythroid element of the marrow. The normal average number of erythroid cells dividing in control animals was about 2.5 per cent. Twenty-four hours after receiving 100 μc of Ca^{45}, the number fell to 0.6 of the control value. It was 0.8 of the normal on Day 2 and 0.4 of the normal by Day 4. On the sixth day after receiving Ca^{45}, the number of erythroid cells in division was slightly above the normal number, but at the end of 2 weeks was 50 per cent below the control values, and remained 25 per cent below the normal at 5 months.

Discussion

The depletion of nucleated cells in the marrow of animals receiving 100 μc of Ca^{45} occurs in 2 stages: (1) a very steep "early" depletion within 24 hours of receiving Ca^{45}; and (2) a less rapid depletion after Day 2 reaching a minimum at 6 days. Marrow differential counts revealed that the largest single loss of cell number in the first 24 hours after receiving 100 μc of Ca^{45} occurred in the mature non-dividing granulocyte pool (65 per cent below normal) and it was the loss of these cells that contributed greatest, although not exclusively, to the "early" fall in the number of nucleated marrow cells. Hulse[5] and others have reported similar decreases in the numbers of mature marrow granulocytes at 6 days after receiving a single dose of 400 r x ray. The animals in these Ca^{45} experiments had received a calculated dose of only 43 rads in 24 hours.

The fact that there was at 24 hours a granulocytopenia concomitant with the decrease in the mature granulocyte pool of the marrow indicates that the decrease in the number of mature marrow granulocytes was not caused by the usual steady release of these mature cells into circulation. It is well known that granulocytes of the blood migrate across the capillary endothelium in random fashion and once into the tissues, where they perform most of their defensive role, do not re-enter the circulation. Be-

cause of radiation-induced cell death within the mature marrow granulocyte pool, the replacement of these migrating granulocytes of the peripheral blood occurs at a reduced rate and, therefore, their number decreases.

It is also possible that some of the mature granulocytes of the marrow moved into the tissue spaces thereby causing a decrease of their numbers in the marrow and in the peripheral circulation; however, no gross infection was evident in the colony and the granulocyte pool in the controls remained normal.

Puck[9–11] has previously presented evidence that in animals receiving from 25 rads to 2,000 rads, nucleated cell depletion is the result of radiation-induced inhibition of cell reproduction rather than cell destruction or accelerated cell removal based on an analysis of single cell survival curves in the marrow of mice that had received total body irradiation. The cell survival curves agreed closely with survival curves produced by mitotic inhibiting agents such as colcemide and vinblastine. We have recently demonstrated[1] that there is in fact a rapid and steep decline in the over-all mitotic index of the bone marrow of rats within 24 hours after receiving Ca^{45} and it remains considerably below normal throughout the first month. Paralleling the decrease in the mitotic index, the number of myeloid and erythroid precursor cells in the marrow shows a transient increase and then a rapid drop to a minimum value at 6 days with only a very gradual recovery to near normal cell numbers at 30 days. It is apparent that radiation has induced mitotic inhibition or delay in the rapidly dividing and differentiating precursor myeloid and erythroid cells. The consequence of the delay is a second later decrease in the number of the nucleated cells of the marrow by Day 6. In other words, it appears that 2 phenomena are responsible for the decrease in number of nucleated marrow cells after irradiation: (1) The "early" fall within 24 hours is the result of radiation-induced cell death and removal especially within the mature granulocyte pool of the bone marrow; and (2) the later fall reaching a minimum at Day 6 is a function of a continued depletion which is no longer compensated for by cell proliferation.

The increase in numbers of myeloblasts, myelocytes and metamyelocytes in the first 3 days after receiving Ca^{45}, even while the total number of nucleated cells is far below normal, may be the result of a shortening of the cell cycle time in the marrow cells. This possibility is presently being investigated in our laboratory.

It is generally agreed that the erythroid element of the marrow is more radiosensitive than that of the myeloid. This is borne out by our results shown in Figure 4*A*. Except for an abortive rise at Day 1 in the 100 μc group, the numbers of nucleated erythroid cells in both treatment groups fall below the controls by Day 2, reach a low point of 20 to 50 per cent below normal at 1 week and remain considerably below normal through 1 month. The unusual finding here is that it is the 25 μc group and not the 100 μc treatment in which the greatest reduction in nucleated erythroid cells is observed. At 5 months the number of erythroid cells in the 100 μc group is still 20 per cent below normal, while the 25 μc group is above normal, thus indicating that the 25 μc treatment retains the greatest potential for recovery in numbers of erythroid cells. The reason that the number of nucleated cells remains below normal in the 100 μc group is shown in Figure 5*B*. The percentage of erythroid cells in division begins to fall by Day 1 after receiving 100 μc of Ca^{45} and with the exception of a return to normal at Day 6 is below normal throughout the 5 months. Therefore, these results indicate the radiosensitivity of the erythroid element to be greater than for the myeloid, but more importantly, under the conditions of low level continuous irradiation employed in this study, the ability of the erythroid cells to recover a somewhat normal mitotic rate is greatly reduced, at least in the larger Ca^{45} treatment dose.

The myeloid complement, on the other hand, recovers normal cell numbers within 2 to 4 weeks after Ca^{45} injection. The per-

centage of the myeloid cells undergoing division is considerably above normal most of the time (Fig. 5*A*).

SUMMARY

The amounts of Ca^{45} used in these experiments were small and the calculated radiation doses through the first 6 days when the most drastic hematologic changes were observed were low compared to x-ray doses used in other experiments to perturb the normal steady state of the bone marrow. Nevertheless, the changes produced within the bone marrow in these rats receiving Ca^{45} were as great, or greater in some instances, as those caused by larger x-ray doses.

Radiation from Ca^{45} incorporated into the bones of the rats, caused cell death and accelerated cell removal within the mature marrow granulocyte pool. Mitotic delay or inhibition of the rapidly dividing and differentiating precursor cells plus the radiation-induced cell death caused a rapid and extensive decrease in the number of nucleated cells of the marrow.

Since there were fewer mature cells in the marrow to cope with natural attrition rates in the peripheral blood, granulocytopenia resulted. Being unable to deliver mature cells for circulation, the marrow released large numbers of immature granulocytes, (bands), and reticulocytes into the blood. Until regeneration in the marrow is relatively advanced, a period follows when immature cells of the marrow predominate.

Recovery approaches normal by 5 months after Ca^{45} injection but cannot be considered to be complete since the Ca^{45} is relatively fixed in the bone and will continue to cause radiation damage. Radium, strontium, and other bone seeking radioisotopes can replace calcium in the bone and can be expected to produce the same relative results in the bone marrow.

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CHANGES IN THE MARROW CELL CYCLE TIME FOLLOWING DEPOSITION OF Ca^{45} IN BONE*

By SAM C. BARRANCO, STEPHEN B. DOTY *and* TIMOTHY MERZ
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SIGNIFICANT amounts (as little as 25 μc) of Ca^{45}, an isotope which is selectively absorbed in bone, have been shown to induce chromosomal damage and mitotic delay in the proliferating cells of the bone marrow of rats.[2] Treatment with 25 μc of Ca^{45} resulted in severe depression of mitosis and a 5 to 7 fold increase in the incidence of fragmented nuclei or micronuclei within 6 to 12 hours following injection of what was effectively a treatment dose of from 2.5 to 5 rads. The incidence of micronuclei increased linearly as the microcurie quantity of Ca^{45} was increased from 25 μc to 300 μc. The incidence of damage was demonstrable throughout the 5 month sampling period.

In addition to the observation of micronuclei, we have quantitated the decrease in the cellularity of the marrow after treatment with Ca^{45}.[3] The decrease was first observable at 24 hours after Ca^{45} injection, and was followed by a subsequent, larger decrease at 6 days. Bone marrow cell differential counts revealed that the "early" decrease in numbers of cells, observed at 24 hours, was probably the result of the combination of radiation-induced cell death within the mature, non-dividing marrow granulocyte pool and displacement of this population of phagocytic cells to other radiation-damaged areas. The later decrease in the number of nucleated bone marrow cells, reaching a minimum at 6 days after Ca^{45} injection, was found to be a function of the continued depletion and death of the dividing and differentiating myeloid and erythroid precursor cells, which were no longer replaced by cell proliferation.

Being unable to deliver mature cells for circulation, the marrow released large numbers of immature granulocytes and reticulocytes into the peripheral blood. Until regeneration in the marrow commenced, a period followed when immature cells of the marrow and the blood were predominant.

Normally, when acute, sublethal, single doses of x- or gamma-radiation are delivered to the hematopoietic tissue, regeneration processes are noted within 6 to 8 days after termination of the radiation treatment.[1] Under conditions of continuous beta-irradiation from Ca^{45} incorporated in the bone, we observed that the marrow cell population showed definite signs of regeneration by the 12th to 15th day after injection of 100 μc of Ca^{45}.

In rapidly proliferating tissues such as bone marrow and small intestine, a decrease in the cell cycle time during continuous irradiation has been reported by Lamerton and Lord,[6] and may be a factor in the process of compensation for cell loss or of regeneration. The experiments in the study presented herein were designed to determine whether regeneration in the marrow was preceded by a shortening of the cell cycle time, and to elucidate the relationship between the incidence of radiation damage and the location of Ca^{45} in the bone.

MATERIALS AND METHODS

The cell cycle times were determined on 3 groups of animals: (1) controls; (2) at 6 days after injection with 100 μc of Ca^{45}; and (3) at 5 months after injection with 100 μc of Ca^{45}. Each group consisted of 30 Sprague-Dawley male albino rats which at the beginning of the experiment were 3 months old and weighed 300 ± 20 grams.

Animals were injected intraperitoneally with 150 μc of tritiated thymidine (specific

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activity of 6.7 c/mM), and bone marrow was sampled at 90 minute intervals for 24 hours. Colcemide (0.4 mg.) was administered intraperitoneally 3 hours prior to killing the animals as a means of collecting dividing cells at metaphase. Slides were prepared as described previously,[2] then coated with liquid K-5 (Ilford) photographic emulsion, stored in light tight boxes at 4°C. and exposed for 1 month. They were then developed with Kodak D-19 developer and mounted with permount. The cell cycle times were determined by counting the labeled metaphases.

Autoradiographs were made of small sections of diaphyseal and epiphyseal bone to determine the location of the Ca^{45} relative to the marrow at various sample times throughout the experiments. The bone tissue was removed at 1 minute, 1 day, 6 days, 15 days, and 5 months after injection of 100 μc Ca^{45} and immediately placed into vials of cold fixative for 18 to 24 hours. Either 6 per cent glutaraldehyde in 0.1 M cacodylate buffer, pH 7.4 at 4°C., or absolute acetone cooled with dry ice was used. Glutaraldehyde-fixed material was dehydrated through a series of alcohols (20, 40, 60, 80, 95, and 100 per cent), propylene oxide and embedded in Epon 812 resin. Acetone-fixed material was freeze dried at −60°C., embedded in hydroxypropylmethacrylate at 4°C.[7] Polymerization of this resin was also completed at 4°C. using an ultraviolet light source.

The blocks of plastic embedded tissue were then sectioned on a Porter-Blum microtome at 1 μ thickness. The resulting sections were positioned on glass slides and dipped into Kodak NTB-2 photographic emulsion. These slides were stored in light tight boxes at 4°C. and exposed for 2 weeks.

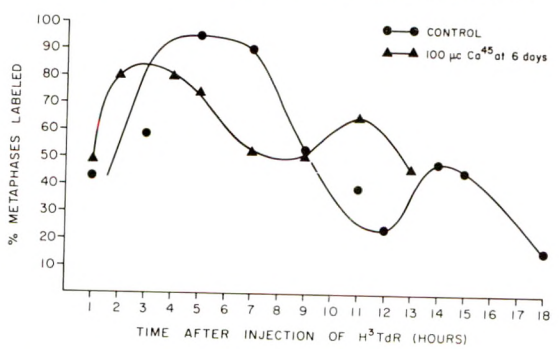


Fig. 1. The marrow cell cycle time at 6 days after treatment with 100 μc of Ca^{45}.

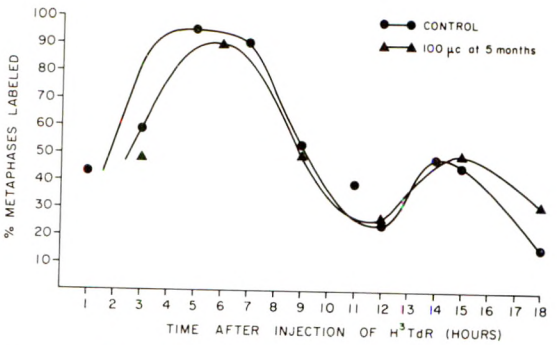


Fig. 2. The marrow cell cycle time at 5 months after treatment with 100 μc of Ca^{45}.

RESULTS

The cell cycle time in the marrow cells of control animals (Fig. 1) was approximately 9.5 hours. Animals receiving 100 μc of Ca^{45} and sampled at Day 6 had a somewhat shorter cell cycle time of approximately 8 hours (Fig. 1).

The cell cycle times for control animals and for Ca^{45} treated animals at 5 months are plotted in Figure 2. They were both approximately 9.5 hours. Each sample point in Figure 1 and Figure 2 represents the average of data obtained from 4 animals.

Figure 3 is an autoradiograph of the metaphysis of the rat tibia showing the reduced silver grains that indicate the presence of Ca^{45} 1 minute after Ca^{45} injection in the mineralized matrix at the lower right portion of the photograph. A zone of unmineralized collagen, a layer of osteoblasts and numerous bone marrow cells can be seen to the left of the mineralized bone.

The dark stippled band running diagonally from upper left to lower right in Figure 4 indicates the location of Ca^{45} in the calcified cortical bone 24 hours after injection with 100 μc of Ca^{45}. The endosteum, and marrow cells can be seen in the upper right portion of the photograph.

Figure 5 shows a very densely labeled

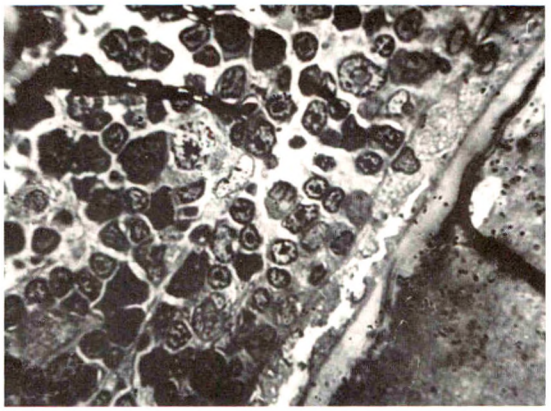


FIG. 3. The location of Ca^{45} in bone with respect to the marrow cells at 1 minute after injection of 100 μc of Ca^{45}.

area within the mineralized matrix of the metaphysis (upper portion of photograph) 6 days after Ca^{45} injection. The decrease in marrow cellularity and the increase in the number of fat cells in this photograph are obvious when compared to the marrow at 1 minute or 1 day after Ca^{45} injection (Fig. 3 and 4). The most severely damaged marrow is, in fact, adjacent to the densely labeled bone in Figure 5, whereas the marrow in the left portion of Figure 5 which is adjacent to only slightly labeled bone, shows little reduction in cellularity.

The histologic section through the metaphysis (Fig. 6) indicates that the Ca^{45} is evenly distributed throughout the mineralized matrix of the bone at 15 days after injection of 100 μc of Ca^{45}. The cellularity of the marrow appears to be reduced to a greater extent than was evident at 6 days (Fig. 5).

Figure 7 demonstrates a section through the cortical bone showing the diffuse Ca^{45} distribution at 5 months after receiving 100 μc of Ca^{45}. After this length of time the Ca^{45} is still present in the calcified bone, although not as dense bands which were evident at earlier sample times. The cellularity of the marrow appears decreased; it is, however, not unlike that of a control animal of the same age. Marrow cellularity does decrease in older animals.[3]

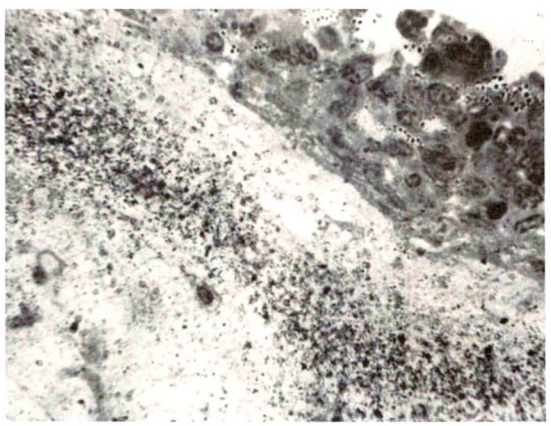


Fig. 4. The location of Ca^{45} in bone with respect to the marrow cells at 1 day after injection of 100 μc of Ca^{45}.

DISCUSSION AND CONCLUSIONS

The cell cycle time that we have measured is a composite cell cycle time. It is not the cell cycle time for a particular marrow cell line, such as the myeloid or erythroid element, but for the dividing marrow population as a whole. Therefore, any changes in this cell cycle time reflect changes

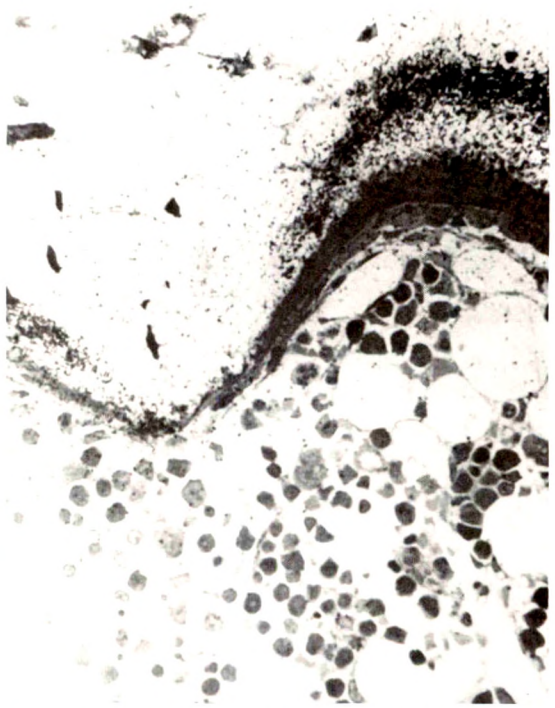


FIG. 5. The location of Ca^{45} in bone with respect to the marrow cells at 6 days after injection of 100 μc of Ca^{45}.

in the over-all marrow mass and not just a particular cell population of the marrow.

The division cycle of a cell has been divided arbitrarily by Howard and Pelc[4] into 4 stages: M, G_1, S, and G_2. Cell division or mitosis is designated as M, and the first gap of time between mitosis and DNA synthesis is designated as G_1. DNA synthesis itself is designated as S, and its length and existence is determined by the uptake of H^3-thymidine. S begins when the uptake of H^3-thymidine begins, and ends when the incorporation of H^3-thymidine stops. The second gap of time between S and M is designated as G_2. Thus, the cell cycle or generation time is that time that it takes for a cell at one stage of the division cycle to move around the cycle and back to its starting point, or as shown in Figure 1, it is the time interval between two corresponding points on the curves. For example, in the control curve, the per cent-labeled metaphases peak first at 5 hours and then exhibit a second smaller peak at 14.5 hours. The control generation time is the difference between 14.5 hours and 5 hours, or 9.5 hours.

The sixth day after Ca^{45} injection was chosen as the time to determine whether changes had occurred in the cell cycle time because: (1) the mitotic index in the 6 day group was 50 per cent below normal and the incidence of micronuclei was 7 times above the control value (Fig. 8); (2) the total number of nucleated marrow cells had reached the lowest value observed during all of the sample periods;[3] and (3) the large numbers of immature cells, once predominant in the blood, had decreased by Day 6.[3] Therefore, the extensive damage evident at 6 days in the marrow and the slight recovery evident in the peripheral blood suggested the beginnings of a recovery period that might possibly be reflected in an alteration in the cell cycle time.

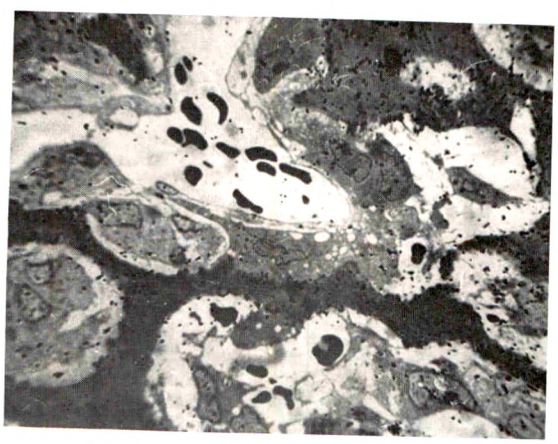


Fig. 6. The location of Ca^{45} in bone with respect to the marrow cells at 15 days after injection of 100 μc of Ca^{45}.

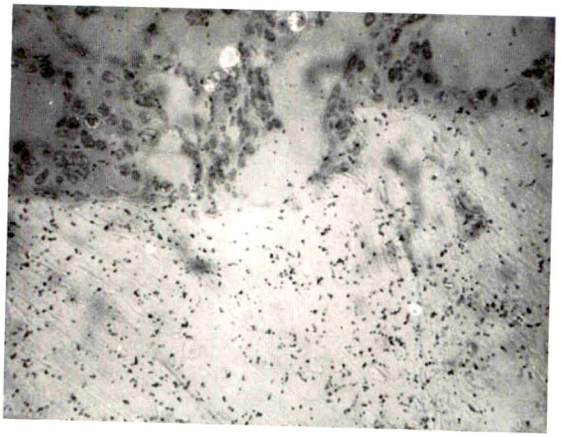


Fig. 7. The location of Ca^{45} in bone with respect to the marrow cells at 5 months after injection of 100 μc of Ca^{45}.

The marrow cell generation time at 6 days after Ca^{45} injection was 1.5 hours shorter than that for control animals (Fig. 1). A decrease in the marrow cell cycle time of rats under continuous irradiation was also observed by Lamerton and Lord[6] and may be a factor in the process of compensation for cell loss and allow the re-establishment of a normal or near-normal steady state in the marrow.

The extent to which the cell cycle time is shortened will depend on the capacity for change in the normal tissue. The myeloid element of the marrow seems to have a greater capacity for recovery than does the erythroid element[3] and seems to benefit the most from the shortened cell cycle time.

Barranco and associates[3] showed that after Day 6 the cellularity of the marrow began increasing toward normal values. At the same time, all of the myeloid cells of

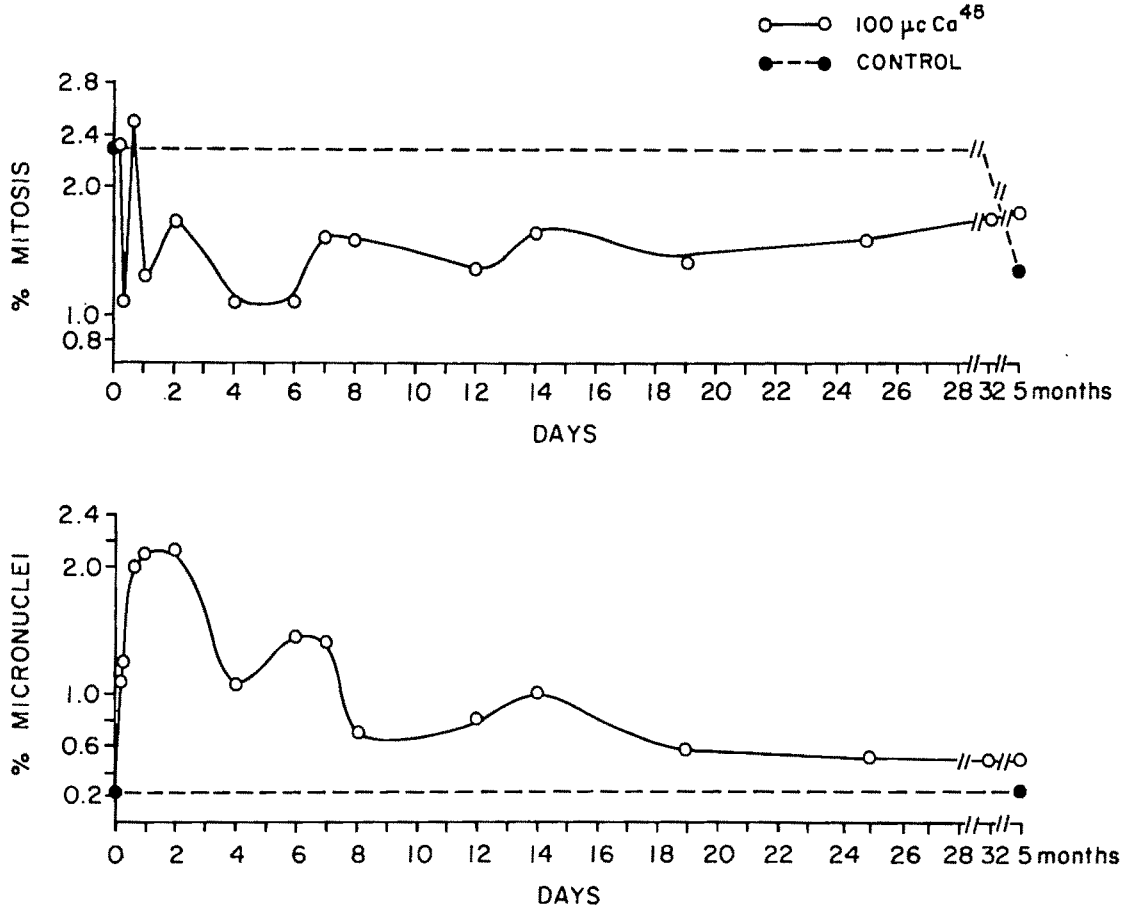


FIG. 8. The mitotic index and the incidence of micronuclei in marrow cells at sample times 4 hours through 5 months after deposition of 100 μc of Ca^{45} in bone.

the marrow and in the blood were also increasing in number toward control values and were near normal or slightly above by 30 days. However, the number of nucleated erythroid cells showed only a slight increase toward normality and remained 25 to 30 per cent below normal through the 5 month sampling period.

Hulse[5] has demonstrated that the erythroid element of the marrow appears more radiosensitive than the myeloid cells; and we have also shown[3] that the number of erythroid cells undergoing division was greatly reduced in animals that received 100 μc Ca^{45} treatment, while the number of dividing myeloid cells was above normal for most of this time. Even though the marrow cell cycle time was a composite measurement, the results indicate that the shortening of the generation time at Day 6 may have been the consequence of an almost complete depression of cell division within the erythroid element of the marrow, while the generation time in the myeloid element remained the same or shortened slightly, thus causing the composite generation time to be shorter. Supporting evidence for this thesis has been presented by Lamerton and Lord[6] who have demonstrated an increase in granulocyte precursor cell proliferation under continuous irradiation.

The cell cycle time in treated animals was normal at 5 months (Fig. 2). The other assay systems tested[3] also indicated an approach toward normality, but recovery cannot be considered to be complete since Ca^{45} is relatively fixed in the bone and, as

shown in Figure 8, results in an incidence of micronuclei greater than controls by a factor of two.

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EXPERIMENTAL STUDIES OF THE SPLANCHNIC CIRCULATION OF THE RABBIT AFTER LIGATION OF THE SUPERIOR MESENTERIC ARTERY*

II: RADIONUCLIDE TRACER STUDIES

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IN EARLIER reports[1,2] we described studies of the angiographic and physiologic aspects of the splanchnic circulation of the rabbit after ligation of the superior mesenteric artery. Briefly, collateral circulation at an aortographically demonstrable level was established almost immediately after ligation, but mesenteric arterial flow waned steadily and disappeared before the death of the animal 8 hours later. Diminution of blood flow did not seem to be the result of clotting, for heparinization failed to affect survival of experimental animals. Certain evidence, reviewed in detail in an earlier publication,[2] suggested that the mechanism of bowel-ischemic death might involve the opening of splanchnic arteriovenous shunts. In support of this contention were the rise in portal venous blood oxygen saturations after ligation, and, of equal importance, a high incidence of contrast material opacification of the portal vein after ligation. Opacification did not appear to be the result of repeated administration of contrast material, when comparison was made with suitable control animals.

Roentgen aortography and selective superior mesenteric arteriography promise to be of great value in the early diagnosis of bowel ischemic states, but some simpler test is required to select appropriate patients for contrast studies. It was our feeling that sufficient alteration might occur in the distribution of the splanchnic blood pool, after interruption of mesenteric arterial flow, to be detectable by the technique of radionuclide blood pool scanning. Accordingly, the following laboratory experiments were carried out.

MATERIAL AND METHODS

SCANNING OF THE ABDOMINAL BLOOD POOL

The experimental subjects were mature albino laboratory rabbits of either sex. Eight animals were used for this phase of the study. The aortographic technique we have previously outlined[2] was followed, and preoperative aortograms of the celiac and splanchnic circulation of each nembutal-anesthetized rabbit were made so that each animal might serve as his own control. The superior mesenteric artery was then ligated, and aortograms were made at irregular intervals from immediate postligation to the premortem state, at about 6 to 8 hours after ligation. These studies were used to demonstrate the establishment of collateral circulation, opacification of the portal vein and similar findings of roentgenologic interest. Before ligation, and either before or after the preligation aortogram, an intravenous dose of 2.0 mc I^{131} HSA (human serum albumin) was injected intravenously into a marginal ear vein. Scanning of the abdomen was carried out with a dual-probe, high-speed rectilinear scanner with two 5 inch Tl-activated NaI crystals and medium-energy focusing collimators. Additional rectilinear blood pool scans were made im-

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† Clinical Fellow of the American Cancer Society, Inc.

mediately after ligation and at hourly intervals until death.

RADIONUCLIDE SCINTIPHOTOGRAPHY OF THE ISOLATED SPLANCHNIC BLOOD POOL

Under nembutal anesthesia the abdomens of 5 rabbits were opened and tiny polyethylene catheters were inserted near the origin of the superior mesenteric artery in such a fashion as not to occlude splanchnic blood flow. A 1.0 mc dose of Tc^{99m} HSA was injected slowly through the catheter and serial exposures were made during injection, and for 3 second intervals thereafter, with a commercial 11 inch crystal scintillation camera of the Anger type. A low-energy grid collimator was used.

In 7 additional rabbits the superior mesenteric artery was catheterized and the artery was ligated proximal to the catheterization site. Through the catheter was injected a dose of 1.0–2.0 mc Tc^{99m} HSA, and serial scintiphotographs were made with an Anger camera during, and at 3 second intervals after, the injection of the bolus. An attempt was made to keep the tracer bolus small in size by using very high specific activity pertechnetate (15.0–25.0 mc/ml.) in the synthesis of the labeled serum albumin; 2.0 mc boluses could be kept within the volume of 0.5–2.0 ml.

RESULTS

SCANNING OF THE ABDOMINAL BLOOD POOL

Figure 1, *A–D* represents a group of rectilinear scans of the abdomen of a rabbit made at intervals after the intravenous injection of 2.0 mc I^{131} HSA. The first scan (Fig. 1*A*) was made under control circumstances on an anesthetized animal and shows the blood pools of the liver (H), the right kidney, and the left kidney (K). Tracer radionuclide may be seen in the midline superimposed within great vessels and low in the pelvis within the bladder. The remainder of the pattern represents the splanchnic blood pool and the superimposed blood pools of the anterior and posterior abdominal walls. The second scan (Fig. 1*B*) was made immediately after ligation of the superior mesenteric artery and shows an augmented blood pool in the left lower quadrant, thought to be due to transfer of blood to the inferior mesenteric arterial circulation in an attempt to establish collateral flow. The scan in Figure 1*C* was made 2 hours after ligation and showed an increase in the counting rate over both lower quadrants and over the right upper quadrant as well, thought to be reflections of collateral flow to the superior mesenteric system. The pattern has changed but little on the fourth scan (Fig. 1*D*), made at 6 hours, just before the death of the animal. This sequence is representative of scans obtained in all 8 animals. On the basis of this experience, abdominal blood pool pattern promises little of value in the selection of patients who may have splanchnic vascular flow abnormalities. However, since patterns in humans may differ from those observed in rabbits, an attempt is being made to evaluate the human abdominal blood pool.

RADIONUCLIDE SCINTIPHOTOGRAPHY OF THE ISOLATED SPLANCHNIC BLOOD POOL

Figure 2, *A*, *B* and *C* represents Anger camera scintiphotographs of the isolated splanchnic blood pool under normal flow circumstances. The first frame (Fig. 2*A*) was made during injection, the second (Fig. 2*B*) at 3 seconds after injection, and the third (Fig. 2*C*) at 6 seconds.

In Figure 2*A*, C represents the escape of Tc^{99m} HSA at the site of insertion of the catheter into the superior mesenteric artery. The bi-lobed pattern beneath it (Fig. 2*B*) represents the distribution of blood in the ileocecocolic (R) and left intestinal (L) segments of the superior mesenteric arterial circulation. In Figure 2*C*, H is thought to represent tracer entering the liver by way of the portal vein.

When Tc^{99m} HSA was injected through a catheter inserted into the superior mesenteric artery distal to a point of ligation, a much different sequence of scintiphotographs was produced (Fig. 3, *A*, *B* and *C*). Figure 3*A*, made during injection, again shows the escape of tracer at C, and early

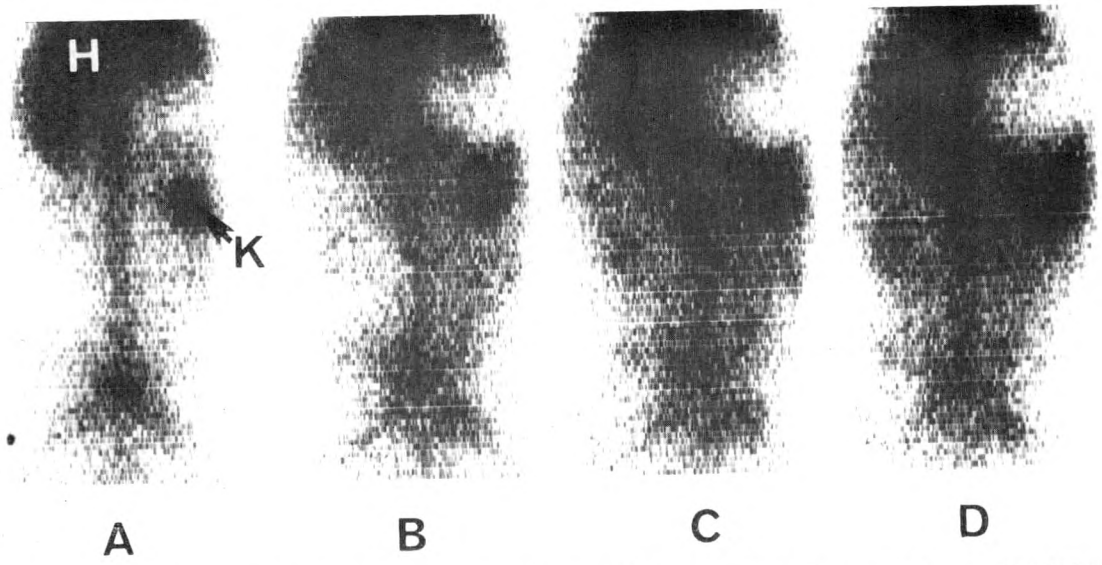


FIG. 1. (*A*) Rectilinear scan of the abdomen and pelvis of a rabbit made after injection of 2.0 mc of I^{131} HSA. H represents the blood pool of the liver superimposing that of the right kidney. K is the blood pool of the left kidney. In the left upper and in both lower quadrants may be seen the normal splanchnic blood pool. Note tracer in great vessels in the abdominal midline and pelvis. (*B*) Rectilinear scan of the abdomen and pelvis of the same rabbit as in *A*, obtained immediately after ligation of the superior mesenteric artery. Note increased radioactivity in the left lower quadrant, possibly representing the blood pool of the inferior mesenteric artery and its branches. (*C*) Rectilinear scan of same animal made 2 hours after ligation of the superior mesenteric artery. There is now increased activity in both lower quadrants. The collateral flow through the abdominal wall may account for part of this, as may leakage of labeled protein through walls of the damaged splanchnic vessels. (*D*) Rectilinear scan, made 6 hours after ligation of the superior mesenteric artery and just before the death of the animal, shows little change in pattern in the 4 hours since the scan seen in *C*.

spread of tracer through the proximal mesenteric circulation is thought to be responsible for the island of activity caudad to this point. Of great interest, however, is the appearance of tracer in what appears to be a channel leading cephalad (P in Fig. 3*A*) toward the liver. Within 3 seconds after injection (Fig. 3*B*) this channel is well defined and the liver (H) is anatomically recognizable. At 6 seconds blood has entered the right heart (HE in Fig. 3*C*).

Confirmation is offered by the experiment in Figure 4. Once again, the individual frames (Fig. 4, *A*, *B* and *C*) were made respectively during, and at 3 and 6 seconds after, injection of a 2.0 mc bolus of Tc^{99m} HSA. Again there is escape of tracer at the site of insertion of a catheter distal to the point of ligation of the superior mesenteric artery. While very little tracer enters the general splanchnic blood pool, there is immediate flow through a channel, P (Fig. 4*A*), in the direction of the rabbit's left upper quadrant. At 3 seconds (Fig. 4*B*) the channel is even better visualized and the outline of a structure resembling the liver is now visible above, and to the left of, the injection site. After conclusion of scintiphotography, the animal was killed and the abdomen was opened widely. An anomalous left-sided liver was present, and the channel corresponding to P in Figure 4*A* was unequivocally the portal vein.

CONCLUSIONS

It is disappointing, but not surprising, to find that blood pool scanning of the whole abdomen does not yield much useful information about changes in the superior mesenteric arterial blood flow. Even though

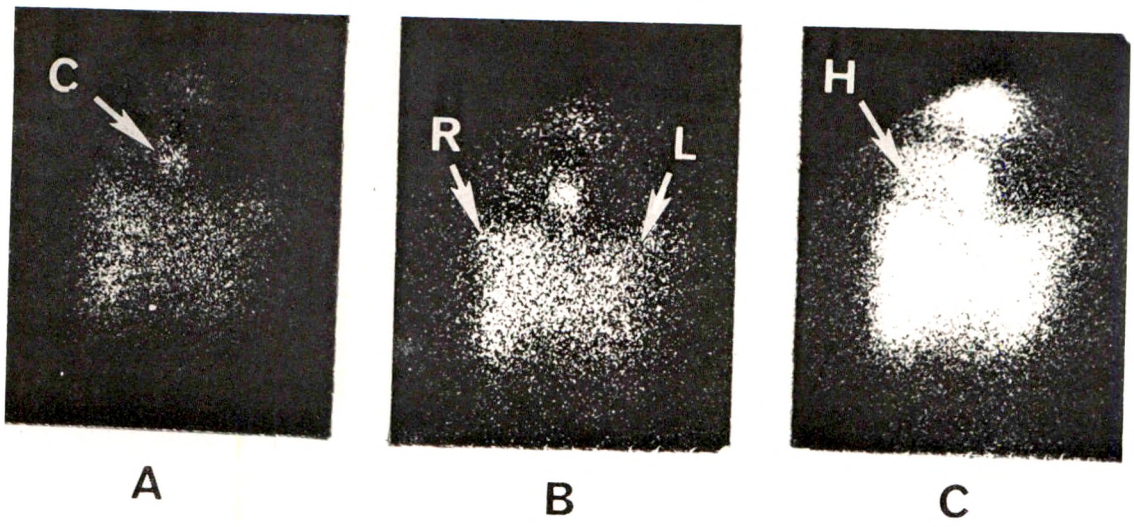


Fig. 2. (*A*) Anger camera scintiphotograph made after injection of 2.0 mc Tc^{99m} HSA through a tiny catheter in place in the unobstructed superior mesenteric artery of a rabbit. C is thought to represent escape of tracer at the catheter insertion site. The catheter was shielded with a small lead tunnel. (*B*) Scintiphotograph made 3 seconds after the scan in *A*. The isolated splanchnic blood pool is seen to greater advantage and assumes a bi-lobed appearance. R is thought to correspond to the ileocecocolic segment and L to the left intestinal segment of the mesenteric arterial circulation. (*C*) Scintiphotograph made 3 seconds after that in *B*. Normal splanchnic blood pool is seen to maximum advantage and tracer is now thought to have entered the liver (H) by way of mesenteric and portal veins.

there is evidence on whole-abdomen scanning which suggests the transfer of blood to collateral pathways after obstruction of the superior mesenteric artery, it is not thought likely that patterns of this sort would be sufficiently obvious in the human to make

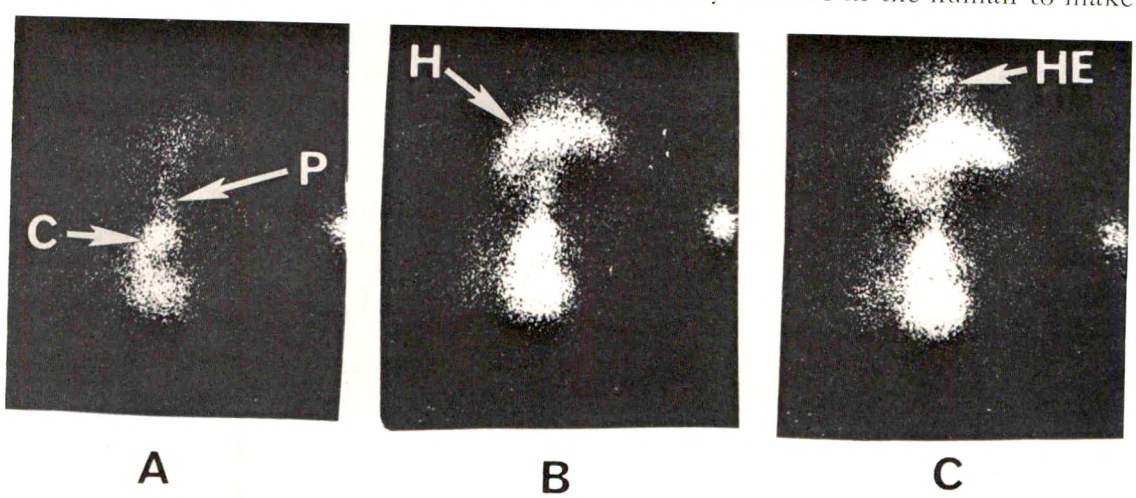


Fig. 3. (*A*) Anger camera scintiphotograph of the abdomen of a rabbit made during injection of 2.0 mc Tc^{99m} HSA. The catheter is in place in the superior mesenteric artery distal to a point of ligation. C represents tracer escaping at catheter insertion site. P is thought to represent the portal vein. (*B*) Scintiphotograph made 3 seconds after that in *A*. Note spread of tracer through proximal aspect of mesenteric circulation and better delineation of the portal vein. Tracer now outlines the liver (H). Note residual tracer in syringe at right of photo. The intervening catheter was shielded by small lead tunnel. (*C*) Scintiphotograph made 3 seconds after *B* shows tracer now entering heart (HE).

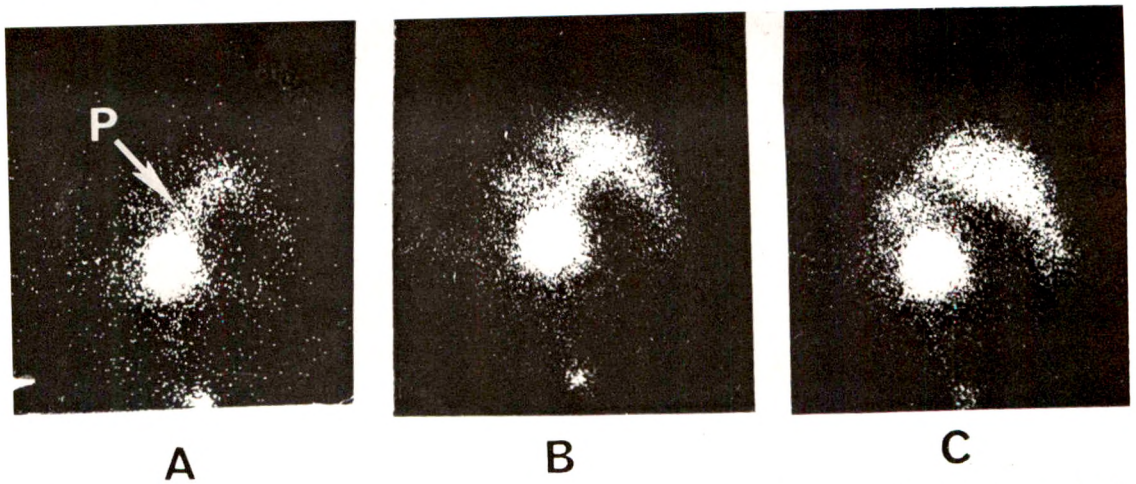


Fig. 4. (*A*) Anger camera scintiphotograph of the abdomen of a rabbit made during injection of 2.0 mc Tc^{99m} HSA through a catheter in place in the superior mesenteric artery distal to a point of ligation. Once again, tracer is thought to be escaping at catheter insertion site, but there is early demonstration of what appears to be a portal vein (P) anomalously directed into the rabbit's left upper quadrant. (*B*) Scintiphotograph made 3 seconds after *A* shows better definition of portal vein and early outlining of the liver. (*C*) Scintiphotograph made 3 seconds after *B* shows more complete outlining of a structure which was found at autopsy to represent an anomalous left-sided liver.

abdominal blood pool scanning a useful screening test to designate patients for selective superior mesenteric arteriography.

We believe that the camera studies described above, showing more immediate entry of undiluted tracer radionuclide into the portal vein, supply another bit of confirmatory evidence for the opening of arteriovenous shunts after ligation of the superior mesenteric artery. It is possible that changes in circulatory dynamics which are the result of altered mesenteric arterial blood flow might be detectable by means of radionuclide tracer flow studies done with a multiple probe system, which would afford a detailed analysis of flow patterns in the regions of the superior mesenteric artery, the celiac axis and the portal vein. Pilot experiments of this sort are now underway in our laboratory.

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ROENTGENOLOGIC MANIFESTATIONS OF MALIGNANT TUMORS OF THE NASOPHARYNX*

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FEW detailed reports of roentgenologic studies of malignant tumors of the nasopharynx have been published, and even fewer have stressed the roentgenologic differential diagnosis of lesions involving this region.

Most malignancies of the nasopharynx are diagnosed clinically, and the main use of roentgenographic studies has been to determine whether, or to what extent, tumor extension has caused osseous destruction.[1–5,7–12] However, clinical diagnosis can be difficult, and the radiologist occasionally may be the first to suggest the diagnosis, either on the basis of a nasopharyngeal soft-tissue mass or of such a mass and adjacent destruction of bone.

Bertolotti,[4] in 1925, and Mayer,[12] in 1928, were the first to emphasize the value of submental-vertical projections of the skull in demonstrating destruction of the floor of the middle fossa, which would otherwise go undetected. Jönsson[7,8] made use of such views in his detailed study of the roentgenologic aspects of pathologic conditions of the nasopharynx. He noted a soft-tissue mass in the nasopharynx on the lateral or submental roentgenograms of the skull in all but 4 of 79 cases of malignant tumor. He noted that malignant lesions were well defined and more ragged appearing on the lateral roentgenograms than were benign conditions. Also, on the submental-vertical projections, benign conditions, with the exception of juvenile nasopharyngeal fibroma, were nearly always in the midline of the nasopharynx, whereas malignant lesions were practically always unilateral. Juvenile fibromas were usually unilateral but were more anterior than were most malignant tumors. Jönsson noted that some soft-tissue masses due to malignant and benign conditions were so similar roentgenographically that he thought that associated bone destructive changes were necessary to make an accurate roentgenographic diagnosis of nasopharyngeal malignant disease.

Godtfredsen[5] made the most extensive study on the sites of bone destruction, as they are manifested roentgenographically. He studied 454 malignant tumors of the nasopharynx. Of the 397 cases in which submental-vertical roentgenograms were made, 29 per cent showed destructive changes. The destruction was adjacent to the nasopharyngeal soft-tissue mass and unilateral in most instances. Although extensive destruction was often present, Godtfredsen found destruction to occur most commonly in three locations: in the region of the foramen lacerum (56 per cent), at the base of the pterygoid process or in the adjacent anterolateral sphenoid sinus (25 per cent), and in the midline (18 per cent).

The purpose of this study was to review and to analyze in detail the roentgenographic findings in 102 cases of primary nasopharyngeal malignant tumor in which roentgenograms were available for study. In addition, to determine criteria for differential diagnosis, roentgenograms were studied in 92 cases of various other conditions in which nasopharyngeal masses, destruction of the middle fossa portion of the base of the skull, or both were present roentgenographically.

MATERIAL AND METHODS

Roentgenograms were available for 102 Mayo Clinic cases in which malignant

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disease was known to originate in the nasopharynx. Cases with extensive involvement of the tonsillar area, pharynx, posterior nasal fossa, palate, or ethmoid region were excluded, unless the primary tumor was known to have originated in the nasopharynx. Stereoscopic submental-vertical projections and routine skull roentgenograms (stereoscopic lateral, Towne, and Caldwell projections) were available in 74 cases. Only routine skull roentgenograms were available in 13 cases, and only submental-vertical projections in 15. Microscopic sections of 81 lesions were available for histologic review.

For the purpose of differential diagnosis, roentgenograms were studied in 92 cases in which other conditions caused roentgenographic evidence of a soft-tissue mass in the nasopharynx or destruction of the floor of the middle fossa, or both.

GENERAL ANALYSIS OF CASES

CLINICAL ASPECTS

Sex and Age. Patients having nasopharyngeal malignant disease—78 male and 24 female—ranged in age from 5 to 83 years, mean 52 years. Fifteen had had radiation treatment before they were seen at this clinic.

Symptoms. Most of the patients had more than one symptom. A lump in the neck was the most common reason for the patient to visit a physician. Other common complaints included aural symptoms (resulting from obstruction of a eustachian tube), headache, symptoms suggestive of cranial nerve involvement, nasal obstruction, and nasal hemorrhage. Headaches were apt to occur at night, suggesting basilar skull involvement to the clinician. Other symptoms included sore throat, foul breath, loss of weight, anorexia, and lassitude. Frequently more than one symptom began at about the same time.

Physical Findings. Clinical descriptions of the tumors were not always detailed. The primary tumor was described as a "mass" in 64 cases, "small lesion" or "slight fullness" in 15, "lesion" in 15, and "cancer of the nasopharynx" in 8.

The most commonly mentioned locations were the concave region between the nasopharyngeal roof and the posterior wall (21 cases), the posterior nasopharynx (16 cases), the region of the fossa of Rosenmüller (10 cases), the nasopharyngeal roof (5 cases), the region of the eustachian orifice (5 cases), pharyngeal recess (4 cases), lateral wall (4 cases), and the anterior nasopharyngeal roof (2 cases). The specific location was not mentioned in the other 35 cases. Most of the described tumors were unilateral, but 19 were bilateral. No mass was present in 4 cases, but a suspicion of malignancy led to biopsy which proved malignant disease to be present. In instances where local extension was described, 3 tumors appeared as masses in the posterior nasal choanal region, and 9 bulged into the oral pharynx.

Cervical lymphadenopathy, usually unilateral on the side of the lesion, was palpable in 50 cases.

Of the 33 patients with neurologic symptoms, 30 were found to have evidence of cranial nerve involvement on initial neurologic examination—most often affecting more than one nerve unilaterally (usually nerves V and VI). Findings of cranial nerve involvement later developed in 10 cases in which initial neurologic findings were negative.

PATHOLOGIC ASPECTS

Because of the highly undifferentiated nature of practically all nasopharyngeal malignant tumors, there probably is less agreement on their classification than on that of any other group of malignant tumors. Most attempts to subclassify them have led, it would seem, to expansion rather than simplification of an already complex nomenclature.

The classifications used at this clinic conform perhaps more closely to those of Yeh[15] than to those of any other author, except that the tumors which we classify in the undifferentiated group were classi-

fied as variants of epidermoid carcinoma by Yeh. He observed that a small specimen may lead to one diagnosis, while a large one may reveal the predominant cell to be of another type.

Of 81 tumors reviewed histologically, 50 were undifferentiated carcinomas, 20 classical squamous cell carcinomas, 9 lymphosarcomas, and 2 cylindromas.

ROENTGENOGRAPHIC ANALYSIS OF CASES

The roentgenograms of the 102 cases of nasopharyngeal malignant tumor were studied with respect to soft-tissue shadows in the nasopharynx and to evidence of osseous involvement.

For this analysis, roentgenograms were divided into 3 groups. Group 1 included both routine and stereoscopic submental-vertical (stereobasal) roentgenograms, available in 74 cases. Group 2 included the routine skull roentgenograms from Group 1 plus roentgenograms from 13 cases in which only routine skull roentgenograms could be obtained, a total of 87 cases. Group 3 included the submental-vertical projections from Group 1 plus roentgenograms from 15 cases in which only stereoscopic submental-vertical projections were available.

NASOPHARYNGEAL SOFT-TISSUE SHADOWS

Nasopharyngeal soft-tissue shadows measuring 1.5 cm. or more on lateral skull projections and discrete masses in the nasopharynx evident on submental-vertical projections, regardless of size, were considered abnormal.

Group 1. In 74 cases with both routine and submental-vertical roentgenograms an abnormal soft-tissue mass in the nasopharynx (Fig. 1) could be identified on either the lateral roentgenograms of the skull or on the submental-vertical roentgenograms in all but 13 cases. Usually (in 49 cases) it could be seen on both of these projections. In the 13 cases with no roentgenographically visible tumor, the clinical description was of a small or flat lesion in most instances. Five of the 13 lesions were described as very large tumors, but they were located against the lateral nasopharyngeal wall or in the region of the fossa of Rosenmüller.

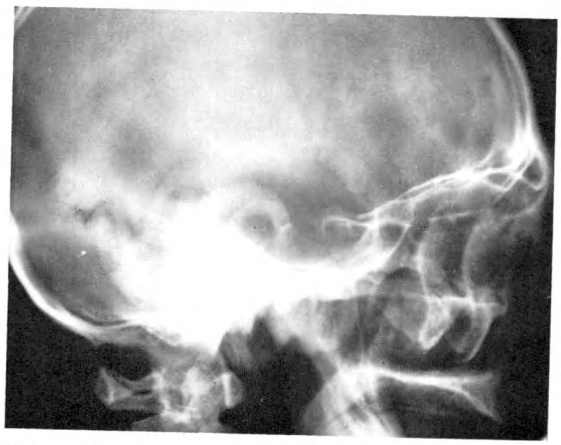


Fig. 1. Squamous cell carcinoma (Grade 2) of the nasopharynx is readily visible as large soft-tissue mass in nasopharynx. Overlying body of sphenoid bone, sphenoid sinus, sella, and clivus show destructive changes.

Group 2. In 87 cases with routine skull roentgenograms, only the lateral projection of the skull was of value in assessing nasopharyngeal soft-tissue densities. An abnormal soft-tissue mass was evident in 65 instances. These were rather subtle findings when they measured from 1.5 to 2.5 cm. in diameter, as they did in 42 cases. The other 23 masses measured 3.0 cm. or more and were large and obvious roentgenographically. In most of the 22 cases in which no tumor was visible roentgenographically, the lesions clinically were flat and small or, if large, were confined to one side of the nasopharynx without crossing the midline. Four patients had no definite tumor clinically; only suspicion of possible tumor led to biopsy. A nasopharyngeal soft-tissue mass was evident roentgenographically in 2 of these cases.

Locations of abnormal soft-tissue masses visible on lateral skull roentgenograms were as follows: vault (44 cases); beneath the roof of the nasopharynx (9 cases); and confined to the posterior wall (4 cases). In 8 instances the mass completely filled the nasopharynx. A downward bulging of the

dorsal surface of the soft palate occurred in 18 cases, where masses were large. The soft palate was markedly displaced downward in 13 of these cases, reducing the volume of the oral cavity. The nasopharyngeal soft-tissue mass could be seen to extend into the posterior choanal region in 4 cases, but this region was often poorly visualized because of the overlapping shadows of the mandible or zygomatic bones.

Group 3. In 89 cases with submental-vertical roentgenograms, a definite soft-tissue mass in the nasopharynx was detectable on these projections in 65 instances. Typically the thickest portion of the mass was readily visible, but the borders were not clearly defined. The mass appeared to be entirely or mainly unilateral, but with slight extension across the midline in 42 cases. Nineteen lesions were large roentgenographically as well as clinically and were bilateral, appearing to occupy all or nearly all of the nasopharynx. In 4 instances, the tumor was confined to the midline of the nasopharynx. The 24 tumors which were not visible roentgenographically were clinically usually small or located far laterally in the nasopharynx.

OSSEOUS DESTRUCTION

Group 1. In 74 cases with routine and submental-vertical roentgenograms, destructive changes were seen in 31 cases on submental-vertical projections but in only 22 of these on routine skull roentgenograms. When destruction was apparent on routine roentgenograms, extensive destruction of the floor of the middle fossa was always seen on submental-vertical projections. When areas of destruction were small, they were seen only on the submental-vertical roentgenograms.

Group 2. In 87 cases with routine skull roentgenograms, 25 cases had evident destruction; the changes were visible only on the lateral skull projections in 12 cases, only on the Caldwell and Towne views in 8 (Fig. 2, *A* and *B*), and on all of these views in 5. The sphenoid bone and sphenoid sinus were involved in all 17 cases in which destruction was visible on lateral skull roentgenograms; in addition, destruction included the sella turcica in 13 cases and the clivus in 10. When osseous destruction was seen on the Caldwell and Towne views, as in 13 cases, it involved a petrous pyramid. The destruction was either confined to

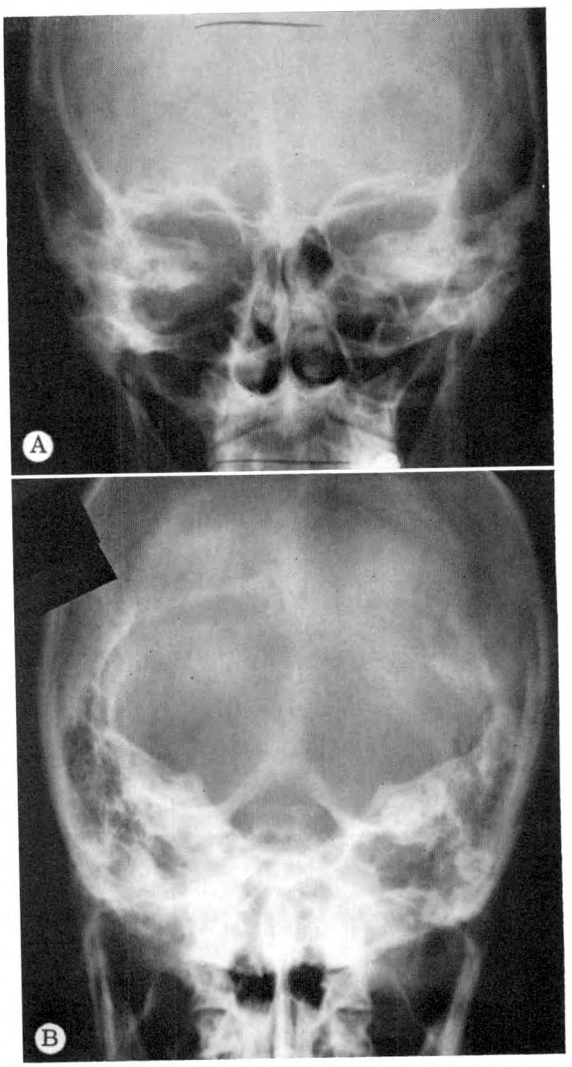


Fig. 2. (*A*) Destruction of inferior aspect of left petrous pyramid by cylindroma. This was the only evidence of destruction seen on routine skull roentgenograms in 8 cases of nasopharyngeal carcinoma. (In submental-vertical projection, destruction mainly involved more of the medial fossa floor.) (*B*) Towne projection of same tumor. Destruction is limited to inferior aspect of the tip of the petrous pyramid on this projection.

the inferior aspect of the tip of the pyramid with the superior surface left intact (9 cases), or the entire pyramid was destroyed but with much more destruction of the inferior than of the superior aspect (4 cases).

Group 3. In 89 cases with submental-vertical roentgenograms, at least some portion of the body of the sphenoid bone and sphenoid sinus appeared destroyed in all 34 cases with evidence of bone involvement (Table 1). Obliteration of at least some portion of the mucoperiosteal margin of the sphenoid sinus, indicating involvement by tumor, and osteolytic change in the adjacent body of the sphenoid bone were observed in all 34 instances (Fig. 3). Thirty of the lesions involved at least one bony margin of the foramen lacerum. Usually the sphenoid bone margins of the foramen lacerum were destroyed, but often other bony margins (those of the basi-occipital portion of the occipital bone and the tip of the petrous pyramid) were included as well.

The site of destruction was mainly unilateral in 18 cases, bilateral in 9, and midline in 7. Although mainly unilateral in 18 cases, the destruction could be seen to extend slightly across the midline in 11 instances. When unilateral, the main focus of destruction was in the region of the foramen lacerum in 13 cases and, more anterior, in the region of the anterolateral sphenoid sinus (including the base of the pterygoid process) in 5 cases. Bilateral destruction was considered to be present when tips of both petrous pyramids and the portion of the floor of the middle fossa between them were involved.

Although the main focus of destruction included the regions mentioned, rarely was destruction confined to one area; practically always adjacent structures also were destroyed. The region of the foramen lacerum was the main site in 13 cases, but extension from one of the other principal sites to include at least one margin of the foramen lacerum occurred in 17 other cases.



Fig. 3. Destructive changes due to lymphoepithelioma of nasopharynx. This submental-vertical projection shows destruction of the most commonly involved sites (body of sphenoid bone, sphenoid sinus, and bony margins of foramen lacerum). In addition, destruction is seen extensively involving the medial aspect of the greater wing of the sphenoid bone on right. Destruction extends farther laterally than usually is seen, and the bony margins of the foramina ovale and spinosum on right are destroyed. The lateral aspect of the sphenoid sinus is invaded by tumor as evidenced by an indistinct mucoperiosteal lateral margin of the sphenoid sinus on the right. Minimal involvement of the body of the sphenoid bone is also seen.

Table I

Region of Osseous Destruction in 34 Cases of Malignant Disease of the Nasopharynx: Roentgenographic Evidence on Submental-Vertical Projections

Region of Destruction	Cases
Sphenoid body and sinus	34
Medial part of greater wing of the sphenoid	30
Back part of body of sphenoid	27
Basioccipital	24
Petrous tip (one or both)	22
Pterygoid process	18
Sella turcica	13
Clivus	10
Foramen ovale and spinosum	6
Vomer	6
Ethmoid sinus	6

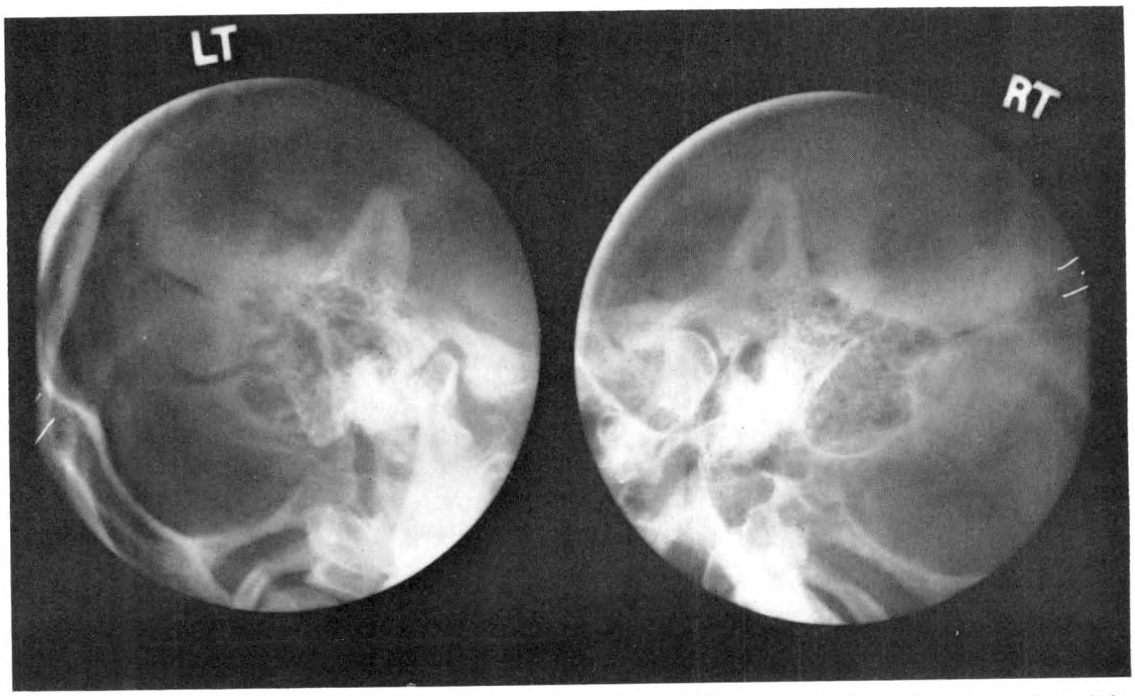


FIG. 4. Same nasopharyngeal carcinoma as in Figure 2, *A* and *B*. Clouding and irregular destruction of the mastoid cell walls can be seen in the Law projection of the left mastoid bone. Right mastoid cells appear normal. (Similar changes were present in 19 of 22 cases that exhibited petrous pyramid destruction.)

Frequently, structures adjacent to the main site of destruction—such as the petrous pyramids, regions of the foramina ovale and spinosum, base of the pterygoid process, sella, clivus, ethmoid sinuses, and vomer—were involved. Extension often included more than one of these.

ASSOCIATED MASTOID ABNORMALITIES

Diffuse clouding of the mastoid cells and loss of clarity or destruction of the cell walls were noted on the roentgenograms of 41 of the 102 patients with carcinoma of the nasopharynx (Fig. 4). The roentgenographic appearance was indistinguishable from that of acute or subacute mastoiditis. Special mastoid views were not obtained in most cases, but these changes were gross enough to be suspected from the routine and submental-vertical roentgenograms of the skull. Changes were on the side of the main nasopharyngeal soft-tissue mass in all instances; in the 9 cases where these changes were bilateral, the soft-tissue mass filled the nasopharynx. Of the 34 cases with evidence of bone destruction, abnormal mastoid changes were seen on the side of the main destruction in 25 instances. Mastoid abnormalities occurred in 19 of the 22 cases with destruction of a petrous pyramid.

COMMENT

Most patients with symptoms of cranial nerve involvement had roentgenographic evidence of osseous destruction. Of the 30 who had signs of such involvement on neurologic examination, all but 9 had associated roentgenographic changes.

DIFFERENTIAL DIAGNOSIS

For the purpose of differential diagnosis, abnormal roentgenograms were studied in a variety of conditions which produce roentgenographic evidence of a soft-tissue mass in the nasopharynx or destruction of the floor of the middle fossa, or both. These roentgenograms represented 92 cases and 19 different pathologic conditions. All diagnoses were verified by biopsy.

Some of the conditions, readily diagnosed clinically, roentgenographically involved not only the nasopharynx and floor of the middle fossa but also, and more extensively, adjacent areas beyond the regions of usual extension of nasopharyngeal malignant lesions. These conditions included extensive malignant tumors of the antrum (2 cases), osteogenic sarcomas (2 cases), and malignant tumors primary in the nasopharyngeal region, but so extensive that the exact site of origin was uncertain (18 cases). The appearance of the 2 osteogenic sarcomas was similar to that seen when these tumors involved other sites.

Most of 7 cases of enlarged adenoids, 2 cases of Thornwaldt's bursitis, and 4 cases of carcinoma of the tonsil or pharynx produced a nasopharyngeal soft-tissue mass which was similar in appearance to that seen in the case of many of the nasopharyngeal malignant tumors; but these conditions, too, were all readily differentiated clinically from carcinoma of the nasopharynx.

Other conditions were at times difficult to differentiate clinically as well as roentgenographically from malignant tumors of the nasopharynx. These included several lesions which presented as soft-tissue masses in the nasopharynx—metastatic melanoma, neurofibroma, and one of the chordomas. Both carcinomas of the sphenoid sinus, 1 chordoma, and 2 meningiomas of the middle fossa floor presented no clinical or roentgenographic findings relative to the nasopharynx, but they had roentgenographic evidences of bone destruction similar to those seen in some cases of nasopharyngeal carcinoma.

The 2 meningiomas (1 was malignant) originated from the floor of the middle fossa and destroyed the inferior aspect of the tip of the adjacent petrous pyramid. This destruction resembled that in the 13 cases of carcinoma of the nasopharynx involving the inferior portions of the tips of the petrous pyramids. Submental-vertical projections were not available in these 2 cases.



Fig. 5. Forward bowing of the posterior wall of the antrum due to juvenile nasopharyngeal fibroma. Posterior wall on side of main tumor mass (right) is bowed forward and uninvolved posterior wall of the left antrum is in a normal position. Posterior ethmoid and sphenoid sinuses are opacified and also were involved by tumor at the time of operation. (Shadow of soft-tissue mass in roof of anterior part of nasopharynx was present in all cases of juvenile nasopharyngeal fibroma.)

In some of the conditions, certain roentgenographic features were helpful in differentiating the lesions from carcinomas of the nasopharynx. These findings are discussed according to the lesion with which they were associated.

Juvenile nasopharyngeal fibroma

The roentgenographic features of these tumors have been reported in detail by Holman and Miller.[6] The typical appearance of most of these tumors was very helpful in differentiating them roentgenographically from malignant disease. The most striking roentgenographic features produced by the slowly expanding and erosive extension of these tumors included: (1) frequent anterior bowing of the posterior wall of the antrum adjacent to the main tumor mass (Fig. 5); (2) erosion through the floor of the sphenoid bone by the tumor, which could be seen on the Waters projection as a well-circumscribed hole with dense bony margins; and (3) occasional enlargement of the superior orbital fissure when the lower outer margin

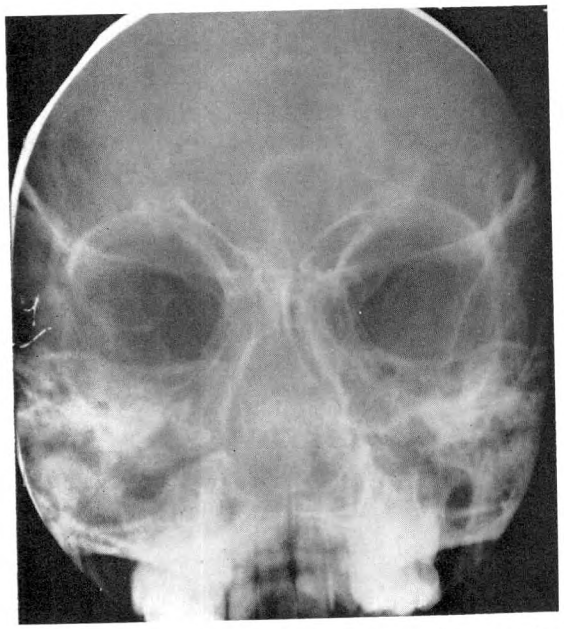


FIG. 6. Erosion and enlargement of the superior orbital fissure. The nasal septum has been displaced by the main tumor mass in the left choanal region. (Left ethmoids and antrum [roof and medial wall] were also invaded by tumor.[6])

of the fissure was eroded by tumor extension (Fig. 6).

A combination of some of the above features, often with evidence of erosion or displacement of other adjacent structures, was highly suggestive of the diagnosis of juvenile nasopharyngeal fibroma in almost every case.

CHORDOMA IN THE REGION OF THE CLIVUS

Five of the 6 chordomas with roentgenographic abnormalities presented features which differed from those associated with carcinoma of the nasopharynx. Each of these five was visible as a soft-tissue mass in the nasopharynx, but the mass was far posterior in the nasopharynx and involved the posterior aspect of the upper part of the oral pharynx as well (Fig. 7*A*). The bone destruction was further posterior than that due to nasopharyngeal carcinoma. The main site of destruction was the clivus, and in all 5 cases the destruction was so far posterior that the anterior margin of the foramen magnum was destroyed (Fig. 7*B*)—a finding not encountered among the cases of nasopharyngeal carcinoma. Two of the chordomas destroyed the anterior aspects of the upper two cervical vertebral bodies.

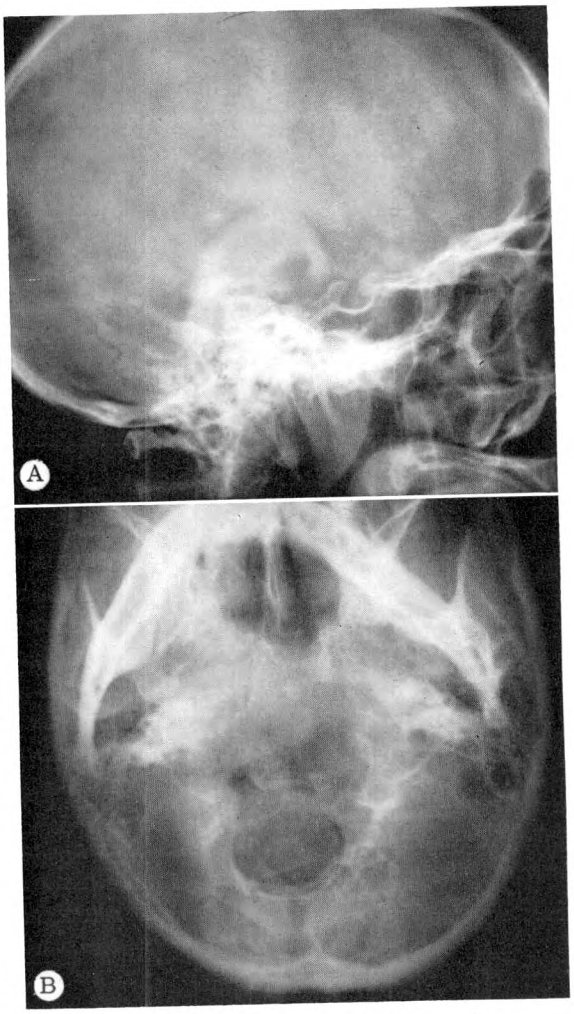


FIG. 7. (*A*) A soft-tissue mass (chordoma) is seen against the posterior nasopharyngeal wall and extending into the posterior part of the oral pharynx. (Five of 6 chordomas exhibited a soft-tissue mass in this location.) (*B*) Submental-vertical projection in same case. Chordoma has destroyed the bony structures much further posteriorly than did any of the nasopharyngeal carcinomas. Destruction of the left side of the posterior portion of the sphenoid bone and the basiocciptal portion of the occipital bone to include the anterior margin of the foramen magnum can be seen as the main site of destruction. (In addition, a portion of the left petrous apex and the anterior aspect of the body of the upper 2 cervical bodies were involved. Five of 6 chordomas destroyed the anterior margin of the foramen magnum.)

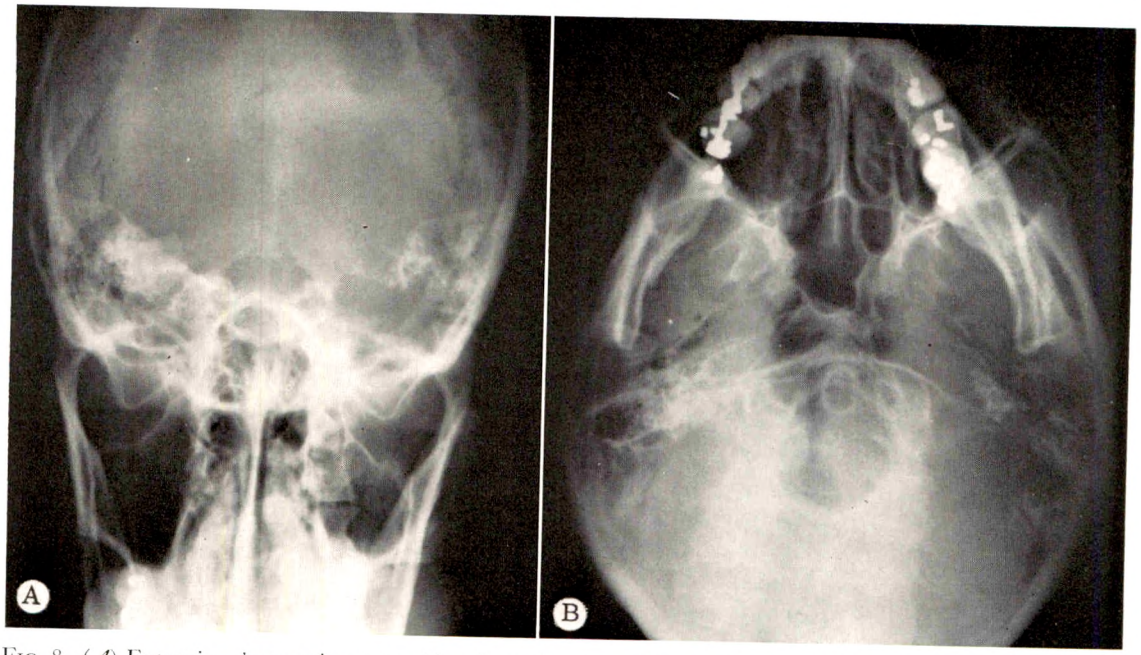


Fig. 8. (*A*) Extensive destruction caused by chemodectoma. (Destruction caused by all of the other chemodectomas was confined to the petrous pyramid.) In this case, destruction extended laterally to involve most of the temporal bone. (None of the nasopharyngeal carcinomas destroyed any of the temporal bone other than the tip of the petrous pyramid.) (*B*) Submental-vertical projection of same case. Principal site of destruction is the temporal bone, especially the petrous portion. Extension posteriorly to involve the occipital bone and medially to include portions of the greater wing and body of the sphenoid bone in the region of the foramen lacerum is seen. The right margin of the sphenoid sinus was also involved. (Main destruction due to nasopharyngeal carcinomas was of the floor of the middle fossa.)

The sixth chordoma, located more anteriorly, involved the body of the sphenoid bone, the sphenoid sinus, and the sella turcica. Roentgenographically, no soft-tissue mass could be seen in the nasopharynx, but the osseous destruction could not be distinguished from that of nasopharyngeal carcinomas in the midline.

Chemodectoma of the Glomus Jugulare

Of the 10 cases of chemodectoma with roentgenographic abnormalities, 7 were previously reported by Rice and Holman.[14] Chemodectomas can diffusely involve the temporal bone and roentgenographically produce a chronic mastoiditis-like appearance. However, occasionally, as in these 10 cases, bone destruction is seen at the inferior aspect of the tip of the petrous pyramid (Fig. 8, *A* and *B*). In none of the 10 cases was a soft-tissue nasopharyngeal mass evident roentgenographically; also, the pattern of osseous destruction, in all cases, was quite different from that associated with tumors of the nasopharynx.

The inferior aspect of the tip of the petrous pyramid was seen to be destroyed (especially in the Towne projections) by all 10 chemodectomas and by 9 nasopharyngeal carcinomas. However, the petrous pyramid represented the most lateral extension of destruction in cases of nasopharyngeal carcinoma, the main destruction occurring more medially, while the petrous portions of the temporal bones were always destroyed as the result of medial extension in cases of chemodectoma.

Involvement of the petrous portion of the temporal bone was associated, in most instances, with abnormal roentgenographic mastoid findings. Usually the mastoid changes in cases of chemodectoma resembled those of chronic mastoiditis; changes in cases of nasopharyngeal carcinoma resembled those of acute or subacute mastoiditis. Chemodectomas dif-

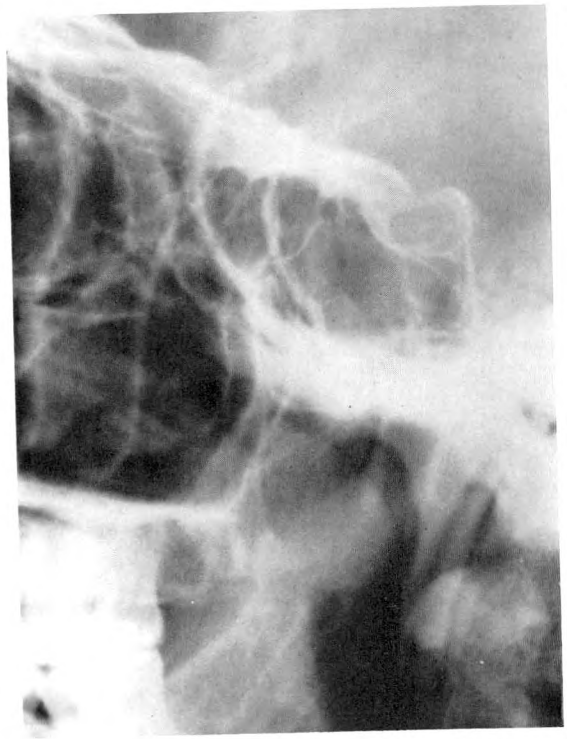


FIG. 9. Choanal polyp seen as a pedunculated mass on the dorsal surface of the soft palate.

fusely infiltrated the temporal bone and filled the mastoid air cells to produce a chronic mastoiditis-like appearance, whereas nasopharyngeal cancers obstructed the eustachian tube, resulting in an acute or subacute mastoiditis-like appearance roentgenographically.

ANTROCHOANAL AND CHOANAL POLYPS

When these polyps protrude into the nasopharynx, they appear entirely different roentgenographically (on the lateral skull roentgenogram) from nasopharyngeal malignant lesions.[13] Each of the 5 polyps studied could be seen as a pedunculated mass lying on the dorsal surface of the soft palate. The posterior aspect of the polyp presented a smooth, convex surface which protruded into the nasopharynx, and a radiolucent zone between the nasopharyngeal roof and the dorsal aspect of the polyp clearly indicated that it did not arise from the nasopharyngeal roof (Fig. 9). The polyps originated in the maxillary antrum. Roentgenographically, the narrow choanal portion of the polyp, leading from the nasopharynx to the ostium of the maxillary sinus, could be seen in only 2 instances; the overlapping shadows of the mandible and zygomatic process obscured this choanal region in the other cases.

SUMMARY

Clinical, pathologic, and roentgenographic findings in 102 cases of malignant disease of the nasopharynx were reviewed, as were abnormal roentgenographic findings in 92 cases of other diseases of the nasopharynx.

Carcinoma of the Nasopharynx. Usually, this could be seen roentgenographically as a soft-tissue mass in the nasopharynx. When both routine and submental-vertical roentgenograms of the skull were available, evidence of osseous destruction was present on the routine views in 22 cases and on the submental-vertical projections in 31. When destruction was visible on routine roentgenograms, extensive destruction of the middle fossa floor was always seen on the submental-vertical projections and usually a large soft-tissue nasopharyngeal mass could be seen on the lateral skull roentgenogram. When bone involvement was visible on the routine skull roentgenograms, usually the changes were seen on the lateral skull roentgenogram; but in 8 instances the only evidence of destruction was present on the Caldwell and Towne views, where the tip of the petrous pyramid, mainly at the inferior aspect, was seen to be destroyed. The destruction seen on the lateral skull roentgenograms involved the sphenoid sinus and body of the sphenoid bone in every instance; in addition, the sella turcica and clivus were often destroyed. On the submental-vertical roentgenograms, in all cases with osseous destruction, some portion of the sphenoid sinus and body of the sphenoid bone appeared to be destroyed. Extension of destruction to include at least one bony margin of the foramen lacerum was seen in 30 of the 34 cases, and extension to other adjacent structures, such as the tips of the petrous pyramids,

the sella turcica, and the clivus, was frequent. Diffuse clouding of mastoid cells was evident in 41 cases.

Differential Diagnosis. Roentgenograms in 92 cases—representing 19 different pathologic conditions characterized by roentgenographic evidence of either a soft-tissue mass in the nasopharynx or destruction of the floor of the middle fossa or both—revealed changes very similar to those of the nasopharyngeal carcinomas in some instances, specifically in cases of enlarged adenoids, Thornwaldt's bursitis, carcinoma of the tonsil or pharynx, metastatic melanoma, neurofibroma, chordoma, carcinoma of the sphenoid sinus, and meningioma of the middle fossa floor. Several of these conditions had either characteristic pathologic or clinical features which differentiated them from nasopharyngeal carcinoma. Juvenile nasopharyngeal fibromas especially could be differentiated from nasopharyngeal malignant tumors. They were located more anteriorly in the nasopharynx than were most of the malignant tumors and in some instances produced highly characteristic features, the most diagnostic of which were: (1) anterior bowing of the posterior antral wall; (2) erosion of a hole through the floor of the sphenoid sinus; and (3) erosion and enlargement of the superior orbital fissure. Chordomas usually produced destruction farther posteriorly than did nasopharyngeal carcinomas. On submental-vertical projections, the destruction seen roentgenographically due to the chemodectomas involved the inferior aspect of the petrous pyramids and adjacent temporal bone, whereas the principal destruction of the nasopharyngeal carcinomas was more medial.

Occasionally the pedicle of the choanal or antrochoanal polyps could be seen leading anteriorly from the mass in the nasopharynx in a rather typical fashion.

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TREATMENT OF CANCER OF THE NASAL CAVITY*

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PRIMARY malignant tumors of the nasal cavity are relatively rare and are usually reported to have a poor prognosis.[3,7,10] Most of the published reports include these tumors in one group with other tumors mainly of the paranasal sinuses.[3–5,8,10,14] The special problems of diagnosis and management of cancer of the nasal fossae[6] and the apparent difference in the prognosis made their separate presentation desirable.[11] In reviewing the literature, the indications for surgery or radiation therapy are not clearly defined and the results of treatment are not easily compared because of the difference in selection of patients for treatment.

In this study, we present the experiences at Roswell Park Memorial Institute in the management of patients with cancer of the nasal cavity. The influence of different prognostic factors on the results of treatment by irradiation and/or surgery will be discussed with an evaluation of the indication for techniques and results of radiation therapy.

MATERIAL

Over the period of 23 years, between January, 1942, and December, 1964, a total of 57 patients with malignant tumors of the nasal fossa were treated at Roswell Park Memorial Institute, Buffalo, New York. The clinical features in the series are presented in Table I. Males were more frequently afflicted than females. The average age incidence was 61 years and 77 per cent of the cases were above 50 years of age. The duration of symptoms varied from weeks to more than 2 years, the average being 8 months. The common early symptoms (Table I) were unilateral nasal obstruction (77 per cent), nasal discharge (54 per cent), epistaxis (40 per cent), and local pain (28 per cent). The remaining symptoms (Table I) were less frequent and usually late.

Chronic sinusitis and nasal polyps preceded the tumor in 8 cases (15 per cent). No other potential predisposing factors, such as benign growths, atrophic rhinitis or previous irradiation, were found.

The tumors were limited to the right side of the nasal cavity in 33 cases (58 per cent), to the left side in 21 cases (37 per cent), and were bilateral in 3 cases (5 per cent). The lateral wall was the most frequent site of tumor: 9 on the tubinates (2—upper, 4—middle, and 3—lower turbinate) and 10 on the rest of the lateral wall. Other sites, in order of decreasing frequency were: septum, vestibule, posterior choana and floor. The site of origin could not be determined in 10 cases with cancer filling the entire nasal cavity (Table II).

These tumors were either polypoidal masses in 38 cases (67 per cent) or ulcerative lesions in 19 cases (33 per cent). Eighteen cases showed extension outside the nasal cavity, mainly to the maxillary antrum (9 cases), ethmoidal sinuses (4 cases), and nasopharynx (3 cases). Lymph node metastases were found in 8 cases (14 per cent) and distant metastases in 2 cases (4 per cent).

Roentgenologic examination of the nose and nasal sinuses showed bone destruction in 18 cases, nasal opacity or mass in 14 cases, and both in 11 cases. Ethmoidal and maxillary sinusitis was seen in 10 cases (Table I).

To assess the importance of the extent of tumor as a prognostic factor, a clinical staging was devised (Table III), based on TNM classification used by Cocchi.[1] Stage

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I (T_1-T_2, N_0, M_0) included 16 cases; Stage II (T_1-T_2, N_1, M_0), 6 cases; Stage III (T_1-T_3, N_2, or T_3, N_0-N_2), 17 cases; and Stage IV (T_4, N_0-N_2 or T_1-T_4, M), 18 cases. T_1 denotes a tumor limited to the mucosa that is 1 cm. in diameter or less; T_2, mucosal lesion more than 1 cm. in diameter; T_3 tumors involving bone or cartilage; and T_4, extension outside the nose. N_1 means a mobile, unilateral lymph node; and N_2 fixed or bilateral lymph nodes. M stands for distant metastases.

The diagnosis was established histologically in all the cases and is given in Table II. The predominant type was squamous cell carcinoma (12—well differentiated, 4—medium differentiated, and 8—undifferentiated, while 8 were ungraded). This was followed by adenocarcinoma (11 cases), mixed salivary tumor (5 cases), anaplastic carcinoma (4 cases) and malignant melanoma (2 cases).

TABLE I

CLINICAL FEATURES

	No. of Patients	Per Cent of Patients
Sex		
Female	12	21
Male	45	79
Age		
Under 40	5	9
40–49	8	14
50–59	7	12
60–69	22	39
70–79	13	23
Over 80 years	2	4
Symptom Duration		
0–2	17	30
2–4	14	25
4–6	8	14
6–12	10	17
Over 12 months	8	14
Presenting Symptom		
Nasal obstruction	44	77
Nasal discharge	31	54
Epistaxis	23	40
Local pain	16	28
Nasal swelling	12	21
Epiphora	5	9
Visual disturbances	3	5
Neck mass	2	4
Tumor Extension		
Maxillary antrum	9	16
Ethmoid sinus	4	7
Orbit	4	7
Nasopharynx	3	5
Sphenoid sinus	2	4
Cribriform plate	1	2
Lymph nodes	8	14
Distant metastases	2	4
Roentgenologic Findings		
Bone destruction	18	32
Nasal opacity or mass	14	25
Both	11	19
Chronic sinusitis	10	17
Negative	4	7

TREATMENT

In this series, three modalities were used as initial treatment: irradiation (30 cases); surgery (13 cases); and combined surgery and irradiation (14 cases) (Table III).

In the irradiation group, 25 cases (57 per cent) received external radiotherapy alone, 10 cases had radium therapy alone and 9 cases were given external irradiation plus radium. Tumors of the vestibule were treated by a single field using orthovoltage radiation. Single anterior fields were used for irradiating other tumors in the anterior part of the nasal cavity. Parallel opposing fields was the technique employed in lesions of the posterior choana while anterior and lateral wedge pair was used in some tumors involving the maxillary and ethmoidal sinuses. In extensive lesions, three cross-firing fields were preferred. Orthovoltage, supervoltage and cobalt 60 equipment were used and the tumor dose was in the range of 5,000 to 6,000 rads in 5–6 weeks depending on the volume treated. In some cases, it was necessary to include the ipsilateral eye in the treatment field, protecting the other eye by lead or by tilting the beam of the lateral fields.

Intracavitary and interstitial radium were used mainly in small tumors limited to the nasal fossa (10 cases). Radium appli-

TABLE II

PATHOLOGY BY ANATOMIC SITES

	Nasal Sites						Total	
	Lateral Wall	Septum	Vestibule	Choana	Floor	Undetermined	No.	Per Cent
Squamous carcinoma	6	12	6	0	0	8	32	56
Anaplastic carcinoma	1	2	0	1	0	0	4	7
Lymphoepithelial carcinoma	0	0	0	2	1	0	3	5
Adenocarcinoma	8	0	0	0	1	2	11	19
Mixed salivary tumor	3	1	1	0	0	0	5	9
Malignant melanoma	1	1	0	0	0	0	2	4
Total Number	19	16	7	3	2	10	57	100
Per Cent	33	28	12	5	4	18	100	

cators or molds were inserted into the nasal cavity through the nostril for anterior lesions or through the posterior naris using a nasal catheter for lesions in the posterior part. Partial excision of the tumor was necessary in some cases to facilitate radium application. Interstitial radium needles or radon seeds were used in 4 patients with accessible anterior tumors of the septum and floor. In cases treated by radium, the tumor dose was 6,000–7,000 rads in 7–8 days depending upon tumor size.

External irradiation plus intracavitary radium was used in 9 cases of locally extensive tumor (Table III). Following external radiotherapy to a tumor dose of 5,000 rads/5 weeks, an intracavitary radium applicator was applied to add 3,000 rads at 0.5 cm. from the surface in 4–6 applications.

The surgical procedures used in 25 cases

TABLE III

INITIAL TREATMENT BY CLINICAL STAGES

	Clinical Stages				Total	
	I	II	III	IV	No.	Per Cent
All Series	16	6	17	18	57	100
Treatment						
Irradiation	11	2	8	9	30	53
Surgery	5	3	3	2	13	23
Combined	0	1	6	7	14	24
Irradiation Techniques						
External irradiation	6	2	6	11	25	57
Radium	5	1	4	0	10	23
Combined	0	0	4	5	9	20
Surgical Procedures						
Local resection	5	3	6	0	14	52
Radical	0	1	3	9	13	48
Combined with Surgery						
Preoperative irradiation	0	0	1	3	4	29
Postoperative irradiation	0	1	5	4	10	71

TABLE IV

RESULTS OF TREATMENT BY CLINICAL STAGES, HISTOLOGY AND SITES
5 YEAR CRUDE SURVIVAL

	A. Clinical Stages				Total
	Stage I	Stage II	Stage III	Stage IV	
Irradiation	8/9 (89%)	1/2 (50%)	2/6 (33%)	1/6 (17%)	12/23 (52%)
Surgery	4/5 (80%)	2/3 (67%)	2/3 (67%)	0/1 (0%)	8/12 (67%)
Combined	—	1/1 (100%)	2/4 (50%)	2/5 (40%)	5/10 (50%)
Total	12/14 (86%)	4/6 (67%)	6/13 (46%)	3/12 (25%)	

	B. Histology						Total
	Squamous Carcinoma	Anaplastic Carcinoma	Lympho-epithelial Carcinoma	Adeno-carcinoma	Mixed Salivary	Malignant Melanoma	
Irradiation	6/12 (50%)	1/4 (25%)	2/2 (100%)	1/3 (33%)	2/2 (100%)	—	12/23 (52%)
Surgery	5/7 (71%)	—	—	1/2 (50%)	2/3 (67%)	—	8/12 (67%)
Combined	3/5 (60%)	—	—	2/4 (50%)	—	0/1 (0%)	5/10 (50%)
Total	14/24 (56%)	1/4 (25%)	2/2 (100%)	4/9 (44%)	4/5 (80%)	0/1 (0%)	

	C. Site					Total
	Lateral Wall	Septum	Vestibule	Choana	Undetermined	
Irradiation	3/6 (50%)	3/6 (50%)	2/3 (67%)	2/3 (67%)	2/5 (40%)	12/23 (52%)
Surgery	3/5 (60%)	4/5 (80%)	1/2 (50%)	—	—	8/12 (67%)
Combined	2/3 (67%)	1/2 (50%)	1/1 (100%)	—	1/4 (25%)	5/10 (50%)
Total	8/14 (57%)	8/13 (62%)	4/6 (67%)	2/3 (67%)	3/9 (33%)	

in this series were simple resection or electrocoagulation of small tumors in 14 cases, and radical resection of the nasal cavity and maxilla with curettage of the ethmoidal and sphenoidal sinuses in the more extensive tumors in 13 patients. Orbital excision was done in 2 cases and radical neck dissection in 4 cases.

In the combined radiotherapeutic and surgical treatment preoperative irradiation was given in 4 cases and postoperative irradiation in 10 cases using radium or external radiation therapy. The dose and the technique depended on the volume of tissue irradiated and were similar to those described above.

RESULTS

Table IV illustrates the results of treatment in the various clinical stages, histology and sites of tumors. Early stages of cancer limited to the nasal mucosa exhibited the best prognosis. Figure 1 and Table IV show that well differentiated squamous cell carcinomas had the best results and that adenocarcinomas had better prognosis than undifferentiated squamous cell and anaplastic carcinomas. Other histologic groups exhibiting good results were the lymphoepitheliomas and mixed salivary tumors. The whole series had a crude 5 year survival rate of 56 per cent, and a higher tumor-free actuarial survival rate of 67 per cent due to the fact that some of the patients were free of tumor at death or follow-up.

In the cases with early stages of this tumor (Stage I and II combined) treated by irradiation or surgery, 5 year survivals of 82 and 75 per cent, respectively, were ob-

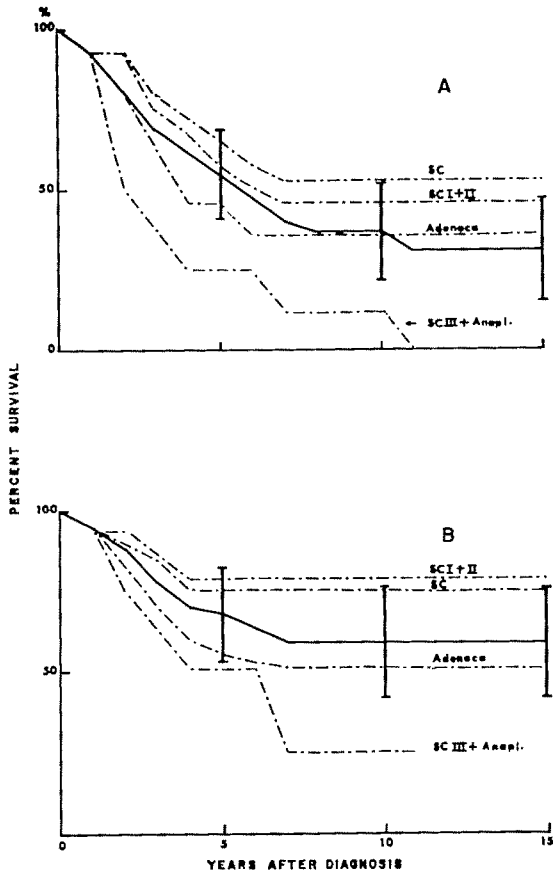


FIG. 1. Survival rate curves after diagnosis of cancer of the nasal cavity. (*A*) Crude survival and (*B*) tumor-free survival. The solid curve is for all cases, the interrupted curve is for the histologic groups and the vertical bars represent 95 per cent confidence interval. SC=squamous cell carcinoma, ungraded. SC I, II and III=squamous cell carcinoma, Grades I, II and III. Anapl.= anaplastic carcinoma.

tained (Table IV). In late stages (Stage III and IV combined) which received radiation, surgical and combined treatments, the 5 year survivals were: 25, 50, and 44 per cent, respectively. Sixteen cases (28 per cent) showed either failure of response (4 cases) or recurrences (12 cases) after the initial treatment. Four of the recurrent cases developed regional lymph node metastases and 2 of them distant metastases. Eighty per cent of the recurrences appeared within the first year after treatment. The mean recurrence time was 10 months. The 4 persistent cases and 5 of the recurrences followed radiation treatment, while 3 recurrences appeared after surgery, and 4 after the combined treatment. All the persistent and recurrent lesions occurred in the patients with an initial advanced tumor of Stages III and IV. Recurrences after initial surgical or combined surgery and irradiation were treated by irradiation. Four of the persistent and recurrent tumors following initial irradiation were re-irradiated and the remaining 5 received surgical treatment.

The final assessment of tumor status showed 5 year cure in 40 cases and failure in 17 cases. The failures include 9 patients with local tumor, 4 with metastases, 1 with both, and 3 of unknown status.

DISCUSSION

The concepts of treatment of nasal cancer differ in the various published studies and change from time to time in the same clinic.[3,9,11] Irradiation, alone, was the primary method of treatment in some series,[5,9] while combined radiation and surgical treatment was advocated in many others.[2,5,10,12–15] Treatment was essentially surgical in some clinics[3,6,7] and either surgical or radiotherapeutic, depending on the radiosensitivity and extent of tumor, in others.[4,8] The wide variations in the reported results can be ascribed to the manner in which the various authors selected cases for treatment and to the type of subsequent analysis.

The treatment methods used in this series depended on the site, extent and the histology of tumor. Radiation therapy was the most commonly used technique in both early and advanced tumors including many epidermoid carcinomas and adenocarcinomas and all anaplastic and lymphoepithelial carcinomas. Surgery was used principally in some of the early cases and in tumors with bone and cartilage involvement and in a few locally extensive tumors, including squamous cell carcinomas, adenocarcinomas and mixed salivary tumors. Combined treatment was selected in advanced lesions of any histologic group.

In the radiation treatment, radium therapy was selected for small accessible lesions; external radiotherapy for larger and less accessible tumors; and radium plus external irradiation in more extensive disease. External irradiation was commonly used as it is more flexible and satisfactory. Parker[11] advocated external roentgen therapy in all his cases. Radium plus external radiotherapy was preferred by Devine *et al.*[2] in nasal and ethmoidal cancer to achieve a homogeneous high lethal tumor dose. However, using supervoltage and cobalt 60 radiation, we can deliver a radical tumor dose without the complications previously reported after conventional radiotherapy.[3] Minor early and late radiation sequelae were reported in some of the cases but no major complications were seen in this series.

Conservative surgery plus irradiation was advocated by Oliver,[10] while more aggressive surgical procedures have been used by Frazell and Lewis.[3] In our cases, selection of simple or radical surgical procedures depended on the site and extension of the tumor.

Because the extent of involvement, site and histology of tumors are important factors in determining survival; these factors will be discussed before the evaluation of the treatment results. Tumor with extension outside the nasal cavity has a poor prognosis.[5,9,10] This is seen in the low survival rates in the advanced stages of this series. Roentgenologic evidence of bone destruction was considered an unfavorable factor in cancer of the nose and paranasal sinuses.[10] However, Larsson and Mårtensson[5] found no great difference between the results in cases with or without bone destruction. In this study, the cases with evident bone destruction and extranasal extension had a shorter survival in all treatment groups. In cases with tumors limited to the naval cavity, presence or absence of roentgenologic evidence of bone involvement produced no difference in the results. The presence of lymph node metastases (relatively uncommon in this series, 14 per cent) was associated with poor prognosis in this material and in others.[5,9]

The location of the tumor has been reported to be of paramount importance.[10] Tumors of the upper and posterior part of the nasal region were reported to have a poor prognosis due to their early infiltration.[5] The influence of a particular site was reported to depend on the ease with which the tumor can extend to a surrounding vital structure; *e.g.*, tumors of the olfactory region may extend to the ethmoids, orbits and base of the skull, while those of the posterior choana spread to the nasopharynx.[8] In this material, allowing for all other possible prognostic factors, no difference existed between the results in tumors of various anatomic sites.

Another prognostic factor is the histologic type. Larsson and Mårtensson,[5] and MacComb and Martin[9] reported bad prognosis in the undifferentiated carcinomas and the adenocarcinomas. On the other hand, Oliver[10] stated that the type of cancer does not appear to alter the prognosis. This series showed a higher survival rate in the differentiated squamous cell carcinomas than in adenocarcinomas. The undifferentiated and anaplastic carcinomas had the lowest survival rate.

The reported results of surgery *versus* radiotherapy in many publications can not be considered as criteria for comparing their respective effectiveness, as surgery was mainly used in early operable cases, while radiation therapy was limited to palliation in inoperable advanced tumors and residual or recurrent disease.[3,4,7] No statistical difference was found among the over-all results of the 3 main methods to treatment in this series. However, the analysis of the results in each stage showed some points of interest. In the early mucosal lesions, both irradiation and surgery gave equally good results. In tumors with bone or cartilage involvement or lymph node metastases the combined and surgical methods apparently yielded better results.

Frazell and Lewis[3] using irradiation in a secondary role in residual or recurrent tu-

mors, reported 18 per cent cure rate after irradiation and 56 per cent after surgery. When comparing their results in the surgical group with the results in this series in the radiotherapeutic group, no difference in the survival rates can be detected. Also, the results in their radiotherapeutic group are comparable to our results in the advanced cases. Hendrick[4] reported 8 cases of nasal carcinoma; 4 early, treated by surgery with 4–7 year survival; and 4 advanced, treated by irradiation with 1–3 year survival. In the series of MacComb and Martin[9] 8 patients survived out of 35 patients with nasal carcinomas treated by irradiation, surgery or combined methods.

Favorable results after radiation treatment of malignant tumors of the nasal fossa were reported by Parker.[11] In 12 patients, he reported a 67 per cent control rate at 3–10 years using external radiotherapy in all the cases.

SUMMARY

Fifty-seven cases of cancer of the nasal cavity were treated initially by irradiation (30 cases), surgery (13 cases) and combined irradiation and surgery (14 cases). Irradiation was given using radium techniques in small accessible lesions, external radiation therapy in less accessible tumors, and external radiation therapy plus radium in more extensive disease. External radiation therapy is the technique commonly used and was considered more flexible and satisfactory. Simple or radical surgical procedures were selected according to the site and extent of tumor. In the combined treatment, surgery was ordinarily followed by irradiation in the treatment of locally advanced tumor.

The degree of extension and the histology of tumor were the most significant prognostic factors. Early well differentiated squamous cell carcinomas have the best prognosis. The 5 year survival in the whole series was 56 per cent. In the early tumors, radiotherapy and surgery gave equally good results. In tumors with bone or cartilage invasion or lymph node metastases, 44–50 per cent 5 year survival followed the combined and surgical treatment.

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ANALYSIS OF CENTRAL RECURRENT DISEASE IN STAGES I AND II SQUAMOUS CELL CARCINOMAS OF THE CERVIX ON INTACT UTERUS*

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CAUSES of death and sites of failure in patients with squamous cell carcinoma of the cervix on intact uterus treated at The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston were recently reviewed by Paunier *et al.*[10] The low incidence of central recurrent disease prompted a detailed analysis of the patients with Stages I and II squamous cell carcinoma of the cervix on intact uterus who had a central recurrence. Some authors[5,6,7] have suggested that there are radioresistant squamous cell carcinomas of the cervix which should be managed surgically rather than by radiotherapy in order to prevent central recurrences. Others[1,12,13] have been less willing to accept the concept of "radioresistance" and have suggested that local failures are related to other factors including inadequate treatment due to poor radium geometry.

MATERIAL

A review was made of 1,341 Stage I and II squamous cell carcinomas of the cervix on intact uterus treated at M. D. Anderson Hospital between the years 1948 and December 1963. Central recurrent disease was defined as clinical or biopsy evidence of persistent or recurrent disease, either on the cervix, in the body of the uterus, or in the upper two-thirds of the vagina at any time of follow-up examination. Patients who had vaginal bleeding of any degree during the terminal phase of their disease were coded as having central recurrent disease. The patients who developed an isolated central recurrence on the cervix or in the upper vagina after being free of disease for 5 years or more were counted in the group of central recurrences.

One hundred and ten patients had a conservative total hysterectomy after slightly less radical radiation therapy as a planned part of their treatment. They were not counted in the central failure group if there was microscopic evidence of residual carcinoma in the hysterectomy specimen. In addition to the fact that the radiation therapy was not as radical because of the planned addition of hysterectomy, Suit and Gallager[14] have shown that the microscopic presence of histologically intact cells does not necessarily constitute evidence of active tumor. Patients who had vault recurrence following irradiation and hysterectomy were counted in the central failure group. If a hysterectomy or exenteration was performed for a central persistent or recurrent lesion after completion of the planned primary treatment, this was counted as a central failure, whether or not the patient subsequently remained free of disease.

Three patients died of intercurrent disease during treatment; 5 patients refused treatment completely, or refused to complete therapy; and 2 patients died of vaginal hemorrhage following small doses of irradiation and hypogastric artery ligation in an attempt to control massive hemorrhage. These 10 patients have been excluded from the analysis of central recurrent disease.

The patients with central recurrences

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were also studied for other sites of active disease. Those who presented with the triad of sciatic pain, leg edema, and hydronephrosis were coded as also having active disease in the regional lymphatics. Patients were counted as having distant metastases if there was clinical, roentgenographic, or autopsy evidence of metastatic disease. Patients with recurrences in the lower one-third of the vagina were coded as having distant metastasis.

The primary lesions of the patients with central recurrences were then studied by different growth patterns. The primary lesions of the portio that infiltrated the fornices or spread into the parametria were separated from the lesions that either arose in the endocervix and expanded centrally or had invaded the myometrium. Lesions which expanded the lower uterine segment to a size greater than 6 cm. in diameter were labeled barrel-shaped lesions and were staged as Stage II.

TREATMENT

The basic plan of treatment of carcinoma of the cervix at the M. D. Anderson Hospital has been outlined in previous publications.[2,3,4] In general, radium alone is used in the Stage I lesions less than 1 cm. in diameter or when only 1 of the 4 quadrant biopsies is positive. Radium plus parametrial irradiation is used in Stage I lesions greater than 1 cm. in diameter, when more than one of the quadrant biopsies is positive, and in early Stage II lesions with favorable anatomy for radium. From 1948 to 1954 the patients with bulky lesions in Stages I and II and the patients with unfavorable geometry for radium received 2,000 to 2,500 r whole pelvis in 3 to 4 weeks using 400 kvp. Since 1954, when a 22 mev. betatron was acquired, it has been the policy to give pre-radium whole pelvis irradiation of 2,000 to 4,000 rads in 2 to 4 weeks to all Stage I and II patients who presented with poor geometry for radium, either because of tumor bulk or because of a narrow vagina or stenotic uterine canal. Selected patients had a conservative total hysterectomy 4 to 6 weeks after the completion of radiation therapy as a planned part of their treatment.

Within this basic treatment plan there has been careful individualization based upon weekly examination and evaluation of the extent of local disease, its response to treatment and the local geometry for satisfactory radium applications.

The treatment charts of all patients with central recurrences were reviewed with particular attention to the roentgenograms of the radium applications. There were only 4 instances of radium source relationship which could have created "cold spots" as an explanation for the central recurrence.

RESULTS

Eight patients out of 471 with Stage I disease and 50 of the 870 patients with Stage II disease have developed central recurrent disease. Analyzing separately the megavoltage period of 1954 to 1963, there has been a 50 per cent reduction in central recurrences both in Stage I and Stage II cases. These data are shown in Table I.

Table II shows the time of central recurrences in Stage I and Stage II. The majority of the recurrences occurred before 2 years. There were 12 recurrences between 2 and 5 years and 9 recurrences 5 years or more after treatment. Six of the 9 central recurrences developing after 5 years had the appearance of new primary lesions. Most of these patients had a well-documented gradual evolution of abnormal vaginal

TABLE I

ALL PATIENTS WITH CENTRAL RECURRENT DISEASE (EITHER ALONE OR IN COMBINATION WITH OTHER SITES) STAGES I AND II CARCINOMA OF THE CERVIX

Stage	Kilovoltage (1948–1954)	Megavoltage (1954–1963)	Total
I (471 patients)	2/64 (3%)	6/407 (1.5%)	8/471 (1.9%)
II (870 patients)	20/252 (8%)	30/618 (4.5%)	50/870 (5.6%)

TABLE II

TIME OF RECURRENCE

(ALL CENTRAL RECURRENCES)

Stage	<2 Years	2–5 Years	>5 Years
I (8)	2	4	2 { 9 yr. Vault recurrence only; exenteration 15 yr. Vault recurrence only; exenteration with localized disease in rectovaginal septum
II (50)	35	8	7 { 6 yr. Vaginal recurrence; NED after radical hysterectomy 8 yr. Central recurrence and pelvic wall 8 yr. Isolated vault recurrence; patient refused exenteration 10 yr. Terminal vaginal hemorrhage—? 10 yr. Vaginal recurrence; NED after exenteration 12 yr. Terminal vaginal hemorrhage—? Previous pelvic wall recurrence 17 yr. Vault recurrence only. Exenteration recently performed; apparently NED at present

smears of Class III to IV for several years with *in situ* biopsies before the final development of a Class V smear, a positive biopsy, or a gross lesion. Five of the 9 patients with late recurrent disease remain free of disease following either radical hysterectomy or an anterior exenteration, and one other patient refused further treatment although she was thought to be a suitable candidate for an exenteration.

In Stage I, there are few central recurrences and they do not appear to be related to any type of growth pattern of the primary lesion. The incidence of central recurrent disease was analyzed with respect to the growth characteristics of the Stage II lesions (Table III). Most of the recurrent central disease is in the group of patients with bulky lesions or endocervical, barrel-shaped lesions; they appeared (34 of 35) within 5 years. In contrast, the uncommon isolated vault failures occurred late, and in patients with relatively early disease.

Table IV shows the other sites of active disease at the time of central recurrence correlated with time of appearance.

Because some of the patients with large endocervical lesions or endocervical lesions with positive endometrial biopsies have received a conservative total hysterectomy

TABLE III

TIME OF RECURRENCE VERSUS TYPE OF INITIAL DISEASE STAGE II

Time of Recurrence	Forniceal Involvement	Parametrial Invasion	Bulky		
			Bulky Cervical Mass, Exophytic, Everting	Endometrial Biopsy Positive	Endocervical Lesion Barrel-Shaped
0–5 yr. (43)	4	5	18	5	11
>5 yr. (7)	5	1	0	0	1
Total	9	6	18	5	12

TABLE IV

STAGE II CENTRAL RECURRENCES SEPARATED BY TYPE OF LESION AND TIME OF RECURRENCE

Time of Recurrence	Forniceal or Parametrial Involvement			Bulky, Everting Exophytic Mass without Lower Uterine Segment Involvement			Barrel-Shaped Endocervical Lesion and/or Positive Endometrial Biopsy		
	Central Alone	Central + Reg.	Central ± Reg. + DM	Central Alone	Central + Reg.	Central ± Reg. + DM	Central Alone	Central + Reg.	Central ± Reg. + DM
<5 yr. (43)	2	5	2	2	6	10		7	9
>5 yr. (7)	5	1						1	
Total		15			18			17	

Note: (1) The majority of the early central recurrences are in the central bulky lesions and the barrel-shaped or endocervical lesions and are associated with pelvic disease and distant metastases.
(2) The late vault recurrences occur in the nonbulky lesions, and are isolated failures. Reg. = regional. DM = distant metastases.

following irradiation in the belief that bulky disease involving the endocervix with invasion of the myometrium (Fig. 1) was more difficult to completely control by radiation, a review was made of all patients having had a hysterectomy as part of the planned treatment for squamous cell carcinoma of the cervix on intact uterus. Table v shows the results in 25 patients with Stage I squamous cell carcinoma of the cervix and 85 patients with Stage II squamous cell carcinoma of the cervix who had a conservative total hysterectomy as a part of the primary treatment of their disease. The Table shows that the endocervical or barrel-shaped type of lesion was the main indication for hysterectomy. In this group of patients central recurrent disease is extremely rare with the majority of the patients dying of distant metastases or intercurrent disease. The fatal complications were not in the conservative hysterectomy group.

In an attempt to answer the question of whether the addition of a conservative hysterectomy following irradiation lowers the incidence of central recurrence, patients with endocervical, expansive, barrel-shaped lesions and the endocervical lesions with

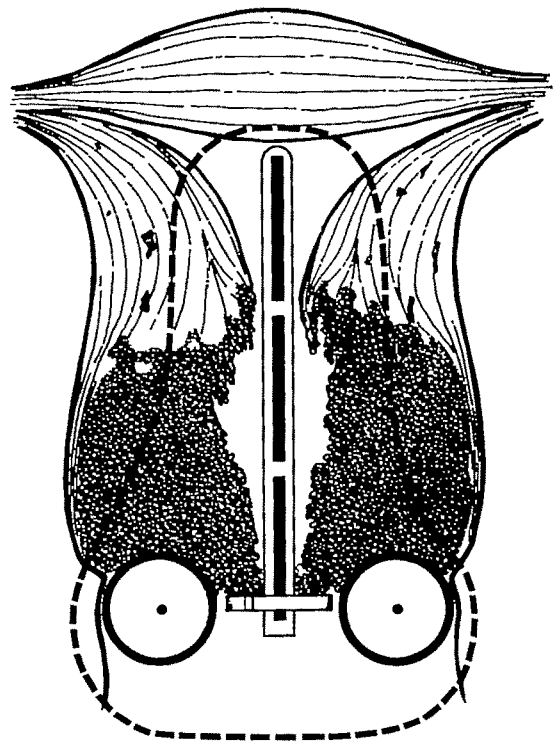


FIG. 1. In the bulky expansile lesion of the endocervix, tumor cells deep in the myometrium are beyond the zone of adequate dosage because of the pear-shaped isodose distribution of the vaginal and intrauterine radium. (Modified from Fletcher, G. H., Textbook of Radiotherapy. Lea & Febiger, Philadelphia, 1966.)

TABLE V

CONSERVATIVE HYSTERECTOMY AS PART OF THE PRIMARY TREATMENT OF STAGES I AND II SQUAMOUS CELL CARCINOMA OF THE CERVIX: 1948—DECEMBER 1963

Stage	Status	Indications for Hysterectomy			
		Endocervical, Barrel-Shaped	Pregnancy	Incomplete Radiation Therapy	Fibroid Other: Pyometria
I 25/471	NED>3 yr.	13/18	2/2	3/3	2/2
	Dead	5/18	0/2	0/3	0/2
	Causes of Death	DM—1 Unk.—1 Comp.—3 Hysterectomy+Lymphadenenectomy—2 Radical Hysterectomy—1			
Total		18	2	3	2
II 85/870	NED>3 yr.	48/69	5/5	3/5	5/6
	Dead	21/69	0/5	2/5	1/6
	Causes of Death	V+PD—2 PD—2 PD+DM—4 DM—7 ID-4 Comp.—1—Bilateral Lymphadenectomy Unk.—1		PD—2	V+PD or necrosis?
Total		69	5	5	6

Note: Table shows all patients who had radiation therapy and simple hysterectomy. Low incidence of central recurrence in patients with bulky lesions.

DM = Distant Metastases; V = Vagina; PD = Pelvic Disease; ID = Intercurrent Disease; Unk. = Unknown; Comp. = Complications; NED = No Evidence of Disease.

positive endometrial biopsy were separated from all other Stage II patients. Patients who had bulky central lesions arising as a polypoid mass were excluded unless the cervix and lower uterine segment were also described as being enlarged. Patients with massive central lesions requiring 5,000 to 6,000 rads total pelvis irradiation prior to radium and patients with extensive parametrial involvement were excluded as they would be unsuitable for hysterectomy.

Using these strict criteria, 133 patients were singled out of the 870 patients with Stage II lesions to contrast the group treated by radiation therapy alone with the group receiving radiation therapy plus hysterectomy.

Table VI shows that the patients who were treated with radiation therapy alone have a higher incidence of central recurrences than those patients having the combined treatment. There were 3 patients in the radiation therapy only group who were scheduled for hysterectomy but failed to return and who subsequently developed a vault recurrence.

DISCUSSION

The incidence of central recurrences in patients with Stage I and II squamous cell

TABLE VI

PATIENTS WITH ENDOCERVICAL BARREL-SHAPED LESIONS OR POSITIVE ENDOMETRIAL BIOPSY
STAGE II

1943–DECEMBER 1963

	NED 3 yr.	Dead	Site of Recurrence or Status of Disease at Time of Death					
			Vault Alone	Vault ± Pelvic Disease ± Distant Metastases	Pelvic Disease Distant Metastases	Intercurrent Disease with Negative Vault	Compli-cations	Un-known
Radiation Therapy Alone (94)	60 (64%)	34	2	12	17	4	0	0
Radiation Therapy + Conservative Hysterectomy (39)	29 (75%)	10	0	1	6	1	1	1

Note: (1) The patients in the table represent a retrospective selection of Stage II patients with bulky central endocervical lesions or lesions with positive endometrial biopsy who would *now* be considered for conservative hysterectomy.

(2) The table shows low incidence of central recurrence in radiation therapy + hysterectomy group (about 3 per cent) *versus* about 15 per cent in radiation therapy alone group. There is about the same incidence of distant metastases in both groups.

carcinoma of the cervix on intact uterus treated at the M. D. Anderson Hospital from 1948 through 1963 is low in comparison with other figures cited in the literature.[1,8,9,12,13] This reflects the individualization of treatment for each patient with carcinoma of the cervix, with the sequential use of whole pelvis irradiation prior to radium for patients with bulky lesions, or with poor radium geometry. The reduction of the central recurrence rate by 50 per cent during the megavoltage period suggests that this more systematic use of whole pelvis irradiation has been an important factor. Careful review of the treatment of these patients reveals that there were no significant under-treatment areas as an explanation for the central failure. Bourne and Mead[1] have suggested that when a standard radium application could not be initially performed in patients with carcinoma of the cervix, this was an indication for surgical treatment rather than radiation therapy. Our data indicate that a more individualized plan of radiation therapy, making the best use of radium, parametrial irradiation, and whole pelvis irradiation, offers an even better chance of lowering the incidence of central failures.

The barrel-shaped lesions, *i.e.*, the endocervical lesion with involvement of the myometrium, account for a high proportion of the central recurrences in Stage II carcinoma of the cervix. The patients with bulky endocervical lesions who had a planned conservative hysterectomy as a part of their treatment have few failures. This is most likely explained by the fact that the radium distribution from the tandem and ovoids is not well suited to treat the expanded disease in the lower uterine segment, as illustrated in Figure 1. The addition of the conservative hysterectomy removes this inadequately treated disease.

The over-all survival rates of these patients is only slightly affected by the hysterectomy, however, as there is a relatively high incidence of regional lymphatic and distant metastasis in this group of patients. The high incidence of regional lymphatic involvement in this group of Stage II patients, who often have inadequately treated disease in the common iliac lymphatics,[11] makes it imperative that high fields be used in the whole pelvis irradiation of these

patients. During the last 2 years, increased use of lymphangiography has led to the realization that many of these patients have extensive common iliac and paraaortic lymph node metastases when initially seen. A pilot program to treat these patients with extended fields to the level of L-4 or even the diaphragm has been initiated in an attempt to improve the survival rates. A prospective, randomized project is also underway to evaluate radiation therapy alone *vs.* radiation therapy plus conservative hysterectomy in the patients with the barrel-shaped Stage II lesions.

The late (over 5 years) isolated central recurrences have the clinical appearance of new primary lesions. There were 13 patients with previously treated carcinomas of the cervix with no evidence of recurrence who developed new lesions of the lower one-third of the vagina that gradually evolved, by the process of dysplastic epithelial changes with atypical cells on Papanicolau smears, to biopsy evidence of carcinoma *in situ*. Several of the patients eventually developed new invasive carcinomas of the lower vagina after many years of follow-up. We suggest that new primary lesions can evolve on the irradiated cervix or in the upper vagina just as they can in the lower vagina following irradiation, or in the vagina following hysterectomy for invasive or *in situ* carcinoma of the cervix.

SUMMARY

1. The central failures in Stage I carcinoma of the cervix are so rare that a definite cause cannot be determined.
2. The majority of central failures in Stage II carcinoma of the cervix occurred in patients who had central bulky disease, endocervical disease, or a positive endometrial biopsy.
3. Almost none of the patients who had a conservative hysterectomy for bulky endocervical disease had central recurrences.
4. There appears to be a small group of patients who developed new *in situ* lesions, either within the treated volume or in the lower vagina, that eventually evolved into a new invasive carcinoma. These were managed either by radical hysterectomy, exenteration, or total vaginectomy, whichever was appropriate. There were instances of long time survivors free of disease following these procedures.

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IRRADIATION OF THE MALE BREAST TO PREVENT HORMONE PRODUCED GYNECOMASTIA*

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HORMONE therapy is now a widely used and accepted treatment in the management of carcinoma of the prostate with metastases. Gynecomastia is an unwanted side effect of this treatment, from both the cosmetic and physiologic point of view. The symptoms of pain and tenderness and a feeling of embarrassment often accompany this problem.

External irradiation of the breasts prior to treatment with diethylstilbestrol has been found to significantly reduce the occurrence of gynecomastia.[1,2,3] Although a great many papers have been published on the subject of gynecomastia produced by the exogenous administration of estrogens, very little has been written concerning the prevention of this problem. The simple procedure of externally irradiating the male breast, prior to beginning hormone treatment, is not a widely accepted practice. It is the purpose of this paper to present our experience with prophylactic irradiation of the male breast.

MATERIAL AND METHOD

Twenty patients with histologically verified adenocarcinoma of the prostate gland were referred to the Department of Radiation Therapy for external irradiation of the breast prior to beginning treatment with diethylstilbestrol. All had clinical and

TABLE I

RESULTS OF EXTERNAL IRRADIATION IN GYNECOMASTIA

Case	Age (yr.)	Follow-up (mo.)	Gynecomastia	Breast Pain	Radiation Skin Change (erythema)	Radiation Skin Discomfort
1	67	10	—	—	minimal	minimal
2	66	28	minimal	minimal	—	—
3	76	30	minimal	—	—	minimal
4	64	14	—	—	—	—
5	58	33	—	—	—	—
6	54	14	—	—	—	—
7	64	8	minimal	minimal	—	—
8	56	19	—	—	—	—
9	69	14	—	—	—	—
10	66	14	—	—	—	—
11	60	19	—	—	minimal	—
12	72	7	—	minimal	marked desquamation	marked
13	66	16	—	—	—	—
14	71	14	—	—	—	—
15	67	29	—	—	—	—
16	58	4	—	—	—	—
17	71	12	—	—	moderate	moderate
18	69	4	—	—	—	—
19	69	10	—	—	moderate	moderate
20	65	10	—	—	—	—

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roentgenographic evidence of metastatic disease.

A surface dose of 900 r was given to each breast in a single dose. The technical factors were as follows: 100 kv.; half-value layer 2.4 mm. Al; focal-skin distance of 22 cm.; and a cone diameter of 5 cm.

RESULTS

Our results are summarized in Table 1. The only complication was the development of a severe skin erythema and desquamation in 1 patient following irradiation.

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RADIATION PROTECTION OF VITAL ORGANS, USING A SELECTIVE ARTERIAL CATHETER*

EXPERIMENTAL AND CLINICAL ASPECTS

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SUCCESSFUL experimental radiation protection of the kidney, employing infusions of epinephrine into the renal artery *via* a percutaneous arterial catheter, has recently been reported by Steckel and co-workers.[4,9] In 4 out of 5 animals surviving for 3 months after acute irradiation of both kidneys to a dose of 1,500 rads, the single kidney infused with epinephrine just before and during irradiation showed striking evidence of radiation protection (Fig. 1). The doses of epinephrine infused into the renal artery (1.2 μg. per minute) were not sufficient to have any systemic effects, and the protected kidney functioned normally prior to sacrifice and was normal histologically.

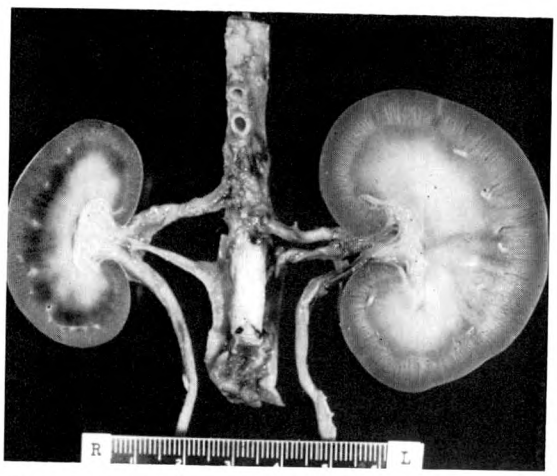


FIG. 1. Sectioned kidneys from a dog which received 1,500 rads in a single treatment to *both* kidneys 3 months before. The larger (left) kidney received an epinephrine infusion into the renal artery, just prior to and during irradiation.

Recently, a pilot clinical investigation has been undertaken in the Clinical Research Center at UCLA in which a limited number of patients with far-advanced malignancies are admitted for intensive radiation therapy to the abdomen and attempted radiation protection of 1 kidney with renal artery epinephrine infusions.[1–4] In addition, experimental studies have focused on an attempt to effect radiation protection of the small bowel in dogs using drug infusions into the superior mesenteric artery *via* a percutaneous catheter.[5,10]

MATERIAL AND METHOD

A. EXPERIMENTAL

In an initial series, total abdominal irradiation or segmental bowel irradiation in the range of 1,000 to 2,000 rads (single dose) was given to several animals, while the superior mesenteric artery was infused *via* a percutaneous catheter with epinephrine (1.3 μg. per minute). No radiation protection of the bowel could be demonstrated in these animals, a finding which may be correlated with the fact that epinephrine alone produces relatively transient vasoconstriction in the superior mesenteric artery.[8] Subsequent electromagnetic flow meter studies in dogs, combined with superior mesenteric arteriograms, con-

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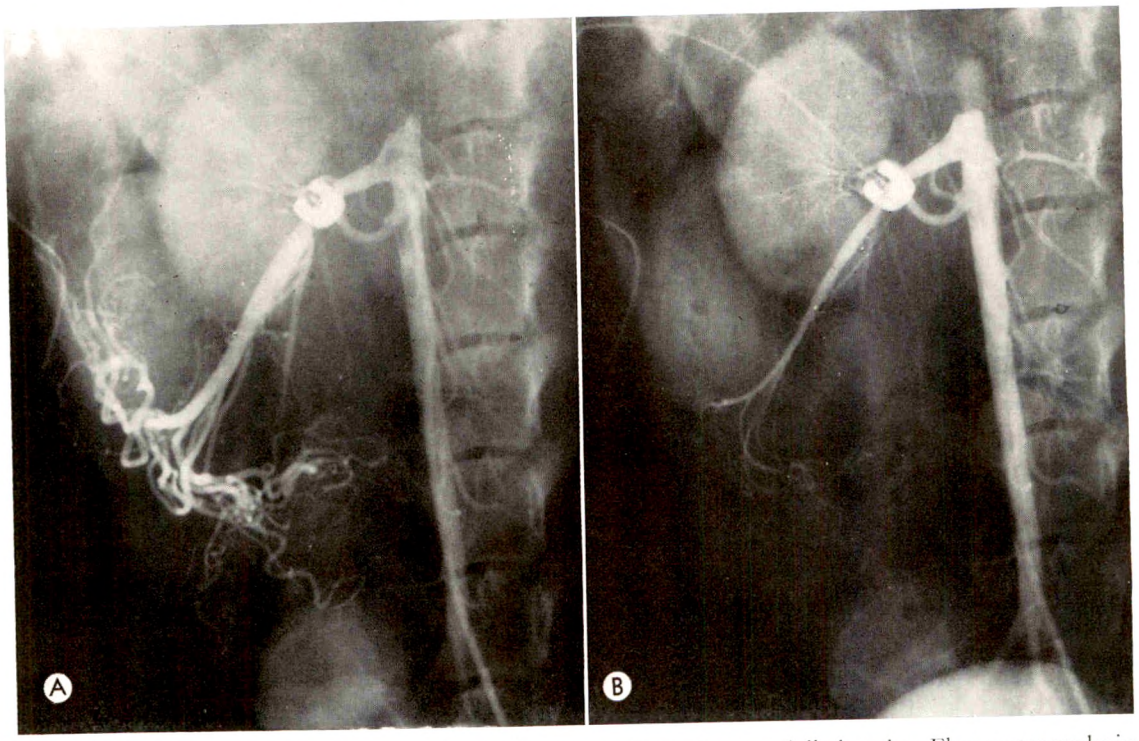


FIG. 2. (*A* and *B*) Two superior mesenteric arteriograms performed sequentially in a dog. Flow meter probe in place, near the origin of the artery. The arteriogram in *A* was performed during a saline infusion into the superior mesenteric artery. The one in *B* was done after a superior mesenteric artery infusion of 2 mg. propranolol, followed by continuous epinephrine infusion (5 micrograms per minute). Note the profound arterial vasoconstriction in *B*, with increased reflux of contrast material into the aorta.

firmed Ross' observation that prior infusion of a beta adrenergic blocking agent (propranolol*), followed by epinephrine, resulted in a more sustained superior mesenteric artery constriction and decreased mesenteric blood flow (Fig. 2, *A* and *B*).[8,10]

Accordingly, in a second series of dogs, 2,000 rads were given to the entire abdomen (5 dogs) while propranolol followed by epinephrine was infused selectively into the superior mesenteric artery (2 mg. of propranolol in 30 cc. saline was infused over 5 minutes, and an epinephrine infusion was then begun at the rate of 5 μg. per minute. Three to 5 minutes later, while the epinephrine infusion was continued, radiation was administered). Six "control" dogs were similarly irradiated, while these drugs were infused nonselectively into the aorta distal to the mesenteric artery, or while saline alone was infused into the superior mesenteric artery.

In a third series of dogs, individual 10 cm. segments of small intestine were irradiated at laparotomy in an attempt to use untreated bowel segments in the same animal as "internal controls": specifically, 2 adjacent mid-small bowel segments were delivered from the animal and suspended above the abdomen. These segments were then irradiated sequentially, using graded acute doses of between 1,000 and 2,000 rads. The first bowel segment in each animal was irradiated during an infusion of saline into the superior mesenteric artery of the animal *via* a percutaneous femoral catheter. The second segment in the same animal was irradiated following infusion of propranolol into the superior mesenteric artery and during an epinephrine infusion (see above). The abdomen was then closed, and small bowel biopsies were performed at

* Supplied as Inderal, by Ayerst Laboratories, New York, New York.

1 week, and again at 1 month after irradiation.

B. CLINICAL

A pilot clinical study of radiation protection of the kidney has been under way at the UCLA Clinical Research Center since August, 1967. Five courses of irradiation have been delivered in 4 patients with far-advanced malignancies, using an indwelling renal arterial catheter for attempted unilateral renal radiation protection (Fig. 3). The catheter is placed percutaneously by the Seldinger technique into 1 renal artery, using an axillary or a femoral artery as the entrance site, and the catheter is kept open between daily epinephrine infusions with a slow infusion of heparinized saline (details to be reported subsequently). Epinephrine is injected daily into the renal artery for 5 minutes before each treatment, and during the radiation treatment, at a rate of 4 μg. to 7 μg. per minute. To avoid local complications of catheterization (infection or thrombosis), no single course of therapy has extended beyond 2½ weeks, at which time the catheter has been removed.

RESULTS

A. EXPERIMENTAL

All 6 control dogs receiving 2,000 rads to the entire abdomen died 4 days to 8 days following irradiation. Pre-terminally, bloody diarrhea occurred, and the bowel was denuded of mucosa at the time of death. Of the 5 test dogs that received infusions of propranolol plus epinephrine into the superior mesenteric artery at the time of irradiation (2,000 rads to the entire abdomen), 3 animals died (3 days, 5 days, and 5 days, respectively, after acute irradiation). However, 2 of the 5 infused animals survived for 6 and 8 weeks, respectively, after irradiation. These 2 animals eventually developed progressive uremia from radiation-induced, bilateral nephritis. Uremia was confirmed by rising blood creatinines before death, and both kidneys showed gross and histologic changes consistent with radiation nephritis.[7]

In the additional series of 4 animals in which adjacent small bowel segments were irradiated sequentially during laparotomy, postirradiation bowel biopsies failed to show any significant difference between the segments of bowel irradiated during drug (propranolol and epinephrine) infusion into the superior mesenteric artery, and the adjacent bowel segments irradiated during saline infusion.

B. CLINICAL

Details of procedure and the preliminary results of the pilot clinical study will be reported subsequently. At the present time, the follow-up period is sufficient in 1 patient for a preliminary evaluation, and this case is reported below.

Report of a Case. R.G., a 58 year old woman, was first seen at the UCLA Medical Center in September, 1967, with a history of an abdominal mass noted 1 month previously. She had been aware of progressive increase in abdominal girth over the past month and had lost about 12 pounds in weight over the last 6 months.

On examination, there was a mass in the lower abdomen arising out of the pelvis, and a left ovarian mass was confirmed on pelvic examination. Preliminary work-up was otherwise negative. Abdominal exploration revealed a pseudomucinous cystadenocarcinoma of the left ovary, with multiple peritoneal implants. She did well in the immediate postoperative period and was discharged, to be admitted 1 month later to the UCLA Clinical Research Center for radiation therapy and attempted unilateral renal radiation protection. The informed consent of the patient was obtained before admission to the study. Following preliminary studies including baseline I^{131} hippuran renograms, renal scintiphotos (hippuran), and an intravenous pyelogram, a catheter was placed percutaneously *via* the left axillary artery, with the tip of the catheter in the patient's left renal artery. A total of 2,077 rads was delivered to the midplane of the abdomen through opposed anterior and posterior portals, over a 15 day period. Cobalt 60 teletherapy was used, and the abdominal portals covered the entire pelvis and abdomen, from the diaphragms to the pelvic floor (24×30.5 cm. field; 100 cm. skin-source distance). Just before each

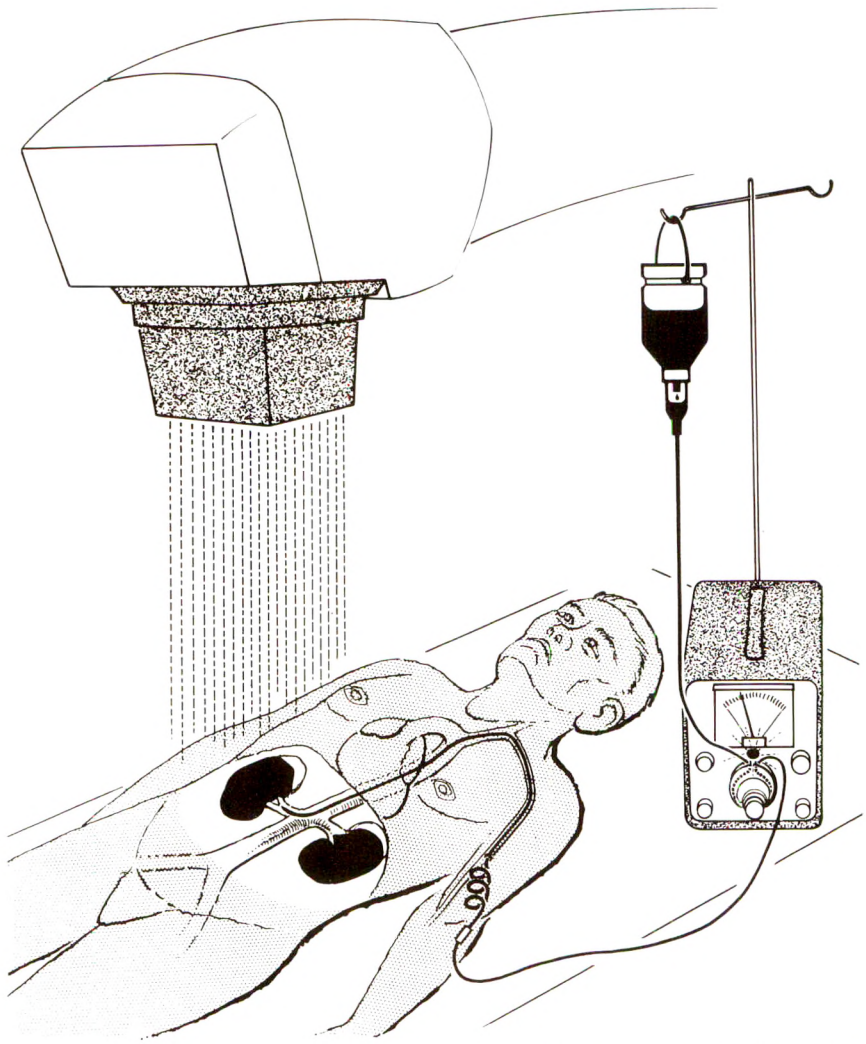


Fig. 3. Schematic representation of treatment situation, with percutaneous renal artery catheter in place. A controlled epinephrine infusion into the renal artery is in progress.

treatment and during the treatment, epinephrine was infused through the left renal artery catheter, at the rate of 4.2 micrograms per minute. The patient experienced moderate left flank pain during each infusion, but the discomfort was not sufficient to warrant routine premedication. Total epinephrine infusion time averaged about 6 minutes daily. Isotope scintiphotography (I^{131} hippuran) of the kidneys was performed during one epinephrine infusion of the left renal artery (Fig. 4, *A* and *B*). Nonuptake of the isotope was demonstrated in the infused left kidney, but immediately following cessation of the epinephrine infusion, uptake of isotope promptly began on the left side. The left renal artery catheter was removed on the fifteenth day following her last radiation treatment, without incident.

After discharge from the Clinical Research Center, she did well clinically, and follow-up isotope renograms and renal scintiphotos, as well as intravenous pyelograms, demonstrated normal renal function bilaterally. She was readmitted electively to the Clinical Research Center 2 months following completion of radiation therapy. The left renal artery catheter was reinserted percutaneously, this time *via* the *right* axillary artery, and an additional 1,500 rads were delivered to the entire abdomen over a 12 day period. As before, daily epinephrine infusions were made into the left renal artery immediately before and during radiation ther-

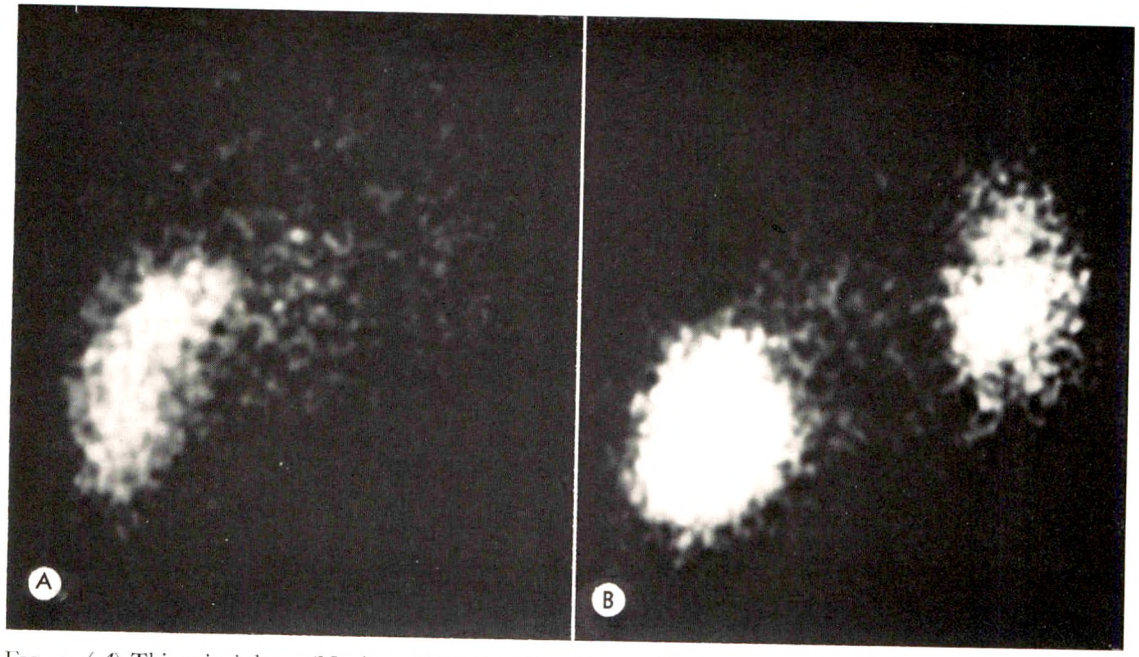


Fig. 4. (*A*) This scintiphoto (Nuclear Chicago, "Pho Gamma") shows non-uptake of I^{131} hippuran by the left kidney, which is receiving an epinephrine infusion into the renal artery *via* a percutaneous catheter. (*B*) Several minutes later, shortly after stopping the selective epinephrine infusion, uptake of isotope by the left kidney begins. (See text.)

apy to the entire abdomen. On this admission, however, the upper third of the left kidney was blocked with lead, both on the anterior and posterior abdominal portals. She tolerated the second course of radiation well, and she was discharged 24 hours after removal of the percutaneous arterial catheter, having received a total of 3,577 rads (midplane) to the abdomen, in 2 courses of therapy over a 3 month period.

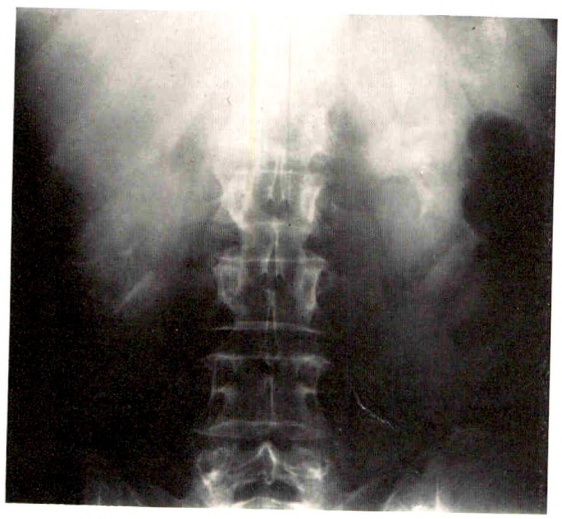


Fig. 5. The 3 minute film from a recent intravenous pyelogram shows an enhanced nephrogram effect *throughout* the left kidney (confirmed on other films from the same study), plus enhanced excretion of contrast material relative to the right kidney. (See text.)

The patient has been followed at regular intervals since discharge and completion of her second course of therapy, and she continues to be asymptomatic. She is working regularly as a school teacher. At this time, 9 months after initiation of radiation therapy and 6 months after completion of her therapy, the intravenous pyelogram is beginning to suggest asymmetry in renal function, the entire left kidney showing a better nephrogram effect than the opposite kidney, and increased density of opaque medium excretion (Fig. 5). This difference has also been reflected on the renogram and on the hippuran scintiphotos. There is no conclusive evidence at this time of tumor recurrence, and blood pressure, serum creatinine, and urinary sediment are normal.

DISCUSSION

In view of previously reported experimental studies, it was thought justified to attempt unilateral radiation protection of the kidney in a highly selected series of

patients with advanced abdominal malignancies.[1–4,6,9] This pilot clinical study is continuing at the present, and the clinical course of 1 patient in whom a preliminary evaluation is now possible, has been outlined. A recent intravenous pyelogram in this patient suggests a possible disparity in function favoring the kidney that was infused with epinephrine during therapy. However, histologic confirmation is not available at the present time, and differential split renal function studies have not been done in view of the patient's favorable clinical course.

Experimental studies in organ radiation protection have concentrated recently upon the investigation of a powerful vasoconstrictor drug combination (propranolol and epinephrine) in the superior mesenteric artery, for small bowel radiation protection.[10] As in the earlier renal studies, a percutaneous catheter has been placed in the feeding artery and vasoconstrictor drugs given just before and during treatment of the radiation-sensitive organ (the small bowel, in this case). Six control animals receiving 2,000 rads to the entire abdomen died within 8 days of irradiation, while 2 out of 5 test animals receiving the same dose during propranolol and epinephrine infusion into the superior mesenteric artery survived acute irradiation only to develop late radiation nephritis. These results are inconclusive, and a larger series will be required to evaluate the significance of these findings, if any. In addition, sequential irradiation of adjacent small bowel segments in laparotomized dogs, both with and without vasoconstrictor drug (propranolol and epinephrine) infusions into the superior mesenteric artery, failed to demonstrate any radiation protection in a drug-infused bowel segment as opposed to a control (saline-infused) bowel segment in the same animal. The reasons for this failure are not clear, but extensive operative manipulation of the bowel with resulting vasoconstriction even in the segments which did not receive propranolol and epinephrine, may be responsible.

Because of the present availability of a powerful vasoconstrictor combination for the superior mesenteric artery and initial encouraging experimental results in renal radiation protection with a percutaneous arterial catheter, further investigations of possible small bowel radiation protection in the intact animal are planned. Future experimental studies of renal as well as small bowel radiation protection will also include protracted and fractionated irradiation with an indwelling arterial catheter. The technique of infusing arterial constrictor substances selectively into a vital organ through a percutaneous catheter, in order to lower the local oxygen tension temporarily and protect the organ from radiation damage will be investigated further in both experimental and clinical situations.

SUMMARY

Experimental attempts to extend the technique of organ radiation protection with a percutaneous arterial catheter to the small bowel, are detailed. Although results to date are inconclusive, further studies are warranted.

Preliminary results from a pilot clinical study of unilateral radiation protection of the kidney are also presented in the form of a case report.

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CELLULAR CHANGES IN THE CONJUNCTIVA AFTER STRONTIUM 90 TREATMENT FOR PTERYGIUM*

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BETA radiation therapy has been commonly used in the field of ophthalmology for a number of years and favorable results have been obtained in pterygium after surgical resection, vernal conjunctivitis, corneal vascularization, limbal tumors, trichiasis, conjunctival papillomas and hemangiomas.[1,5–8,13,22] Complications resulting from beta irradiation have been studied and reported by Merriam[16] and others[1,8,13,15,19] (Table 1). The appearance and behavior of daughter cells derived from the cells being irradiated during therapy are not yet known, but with the increasing popularity of strontium 90 for the treatment of benign conjunctival diseases, an investigation of the cellular changes of the conjunctiva after radiation therapy seemed necessary.

MATERIALS AND METHOD

Patients who received beta irradiation for the treatment of pterygium postoperatively at Bellevue Hospital were chosen for study. From 1953 there have been 950 cases of pterygium treated with Sr^{90}. From this group, 62 patients were selected for this study. Each patient was carefully investigated to include age, sex, race, location of pterygium, time of operation, time of radiation therapy, total dosage and the results of treatment. Naked eye and slit-lamp examinations of the conjunctiva, cornea, iris and lens were done prior to cytologic study. The irradiated conjunctiva was scraped with a platinum wire loop. The opposite untreated eye was used for control. Care was taken to avoid scraping the cornea. Smears were stained with Giemsa stain[2] and the cells studied periodically to minimize the possible omission of significant findings.

TECHNIQUE OF SR^{90} TREATMENT

In the 1930s and 40s at Bellevue Hospital, pterygia were treated with a radon applicator. In 1953 this was replaced by a Tracerlab applicator containing 50 mc of strontium 90.[13] Treatments were started on the third or fourth postoperative day. The affected eye was anesthetized with 1 per cent pontocaine or 0.5 per cent ophthaine for about 15 minutes. With the patient in the supine position, the lids were separated by a retractor as wide as comfort permitted. The patient was instructed to fix the eye in one direction by looking at the index finger held up by the physician. The Sr^{90} applicator was placed directly on the limbus of the cornea where the head of the pterygium was severed surgically (Fig. 1). The treatment time of 25 seconds yielded 1,000 reps on the surface of the conjunctiva. Corticosteroid ointment was applied and a pressure bandage was placed on the eye to be kept for 2–4 hours after treatment. The patient was instructed to wear wide-frame dark sunglasses during the day to eliminate photophobia. The same treatment was repeated at weekly intervals for a total of 3 treatments (3,000 reps). This scheme has been used routinely in every patient since 1956. The original dose schedule, from 1953 to

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TABLE I*

LATE EFFECTS OF BETA RADIATION ON THE EYE

Complications	Surface Dose (rep)	Duration after Therapy
A. *Conjunctiva*		
Telangiectasis	3,000– 5,000	5 years
Keratinization of epithelium	5,000–10,000	
B. *Sclera*		
Atrophy	20,000–30,000	
C. *Cornea*		
Superficial punctate keratitis	5,000	Transient effect
Vascularization	20,000–30,000	up to 12 years
Scarring	25,000	
D. *Uvea*		
Iritis	22,000–27,000	
Iris atrophy	20,000–30,000	
E. *Lens*		
Radiation cataract	2,300–22,000	3–6½ years in 7/8 cases;
(Calculated dose at 3 mm. depth . . .	230– 1,120)	13 years or more in 1/8 cases

* From Merriam, G. R. Jr.[16]

1955, was to deliver a total dose of 5,000 reps given in 2 treatments 1 week apart.

PHYSICAL CHARACTERISTICS OF SR^{90}

Strontium 90 is a fission product[6,9,13] with a long half life of 28 years.[9] It decays by emitting beta particles of 0.54 mev. peak, into yttrium 90, which in turn decays, with a half life of 64 hours, into a stable zirconium 90 by emitting a more powerful beta ray of 2.27 mev. peak. This energy is as much as 4 times the energy produced by the strontium 90. There is no gamma emission from either Sr^{90} or Y^{90}. The Sr^{90} in the Tracerlab applicator is filtered by a shell composed of 0.002 mm. stainless steel plus 0.01 mm. aluminum. The diameter of the applicator is 1 cm. The half value layer (H.V.L.) of the filtered Sr^{90} is about 0.9 mm. of soft tissue.[6] The equator of the lens lying 4 mm. beneath receives 4–6 per cent of the surface dose.[8,9,10] Therefore, the lens will receive about 150 reps when 3,000 reps is given to the surface of the limbus. The rep (roentgen equivalent physical) represents an energy absorption of 93 ergs per gram of tissue. Recently, a new unit of absorbed dose in tissue, rad, has been adopted, which yields 100 ergs per gram of tissue after absorption of the energy. By converting the rep to rad, 1 rep equals 0.93 rad, or 1 rad equals 1.075 rep.[8]

RESULTS

The age incidence of patients with pterygium ranged from 18 to 73 years. The common age was from 21 to 50 years (Table II). Thirty-six of the 62 patients were male (56 per cent). Eighty-seven per cent were Puerto Rican, 8 per cent white, and 5 per cent Negro. There were 78 eyes affected in

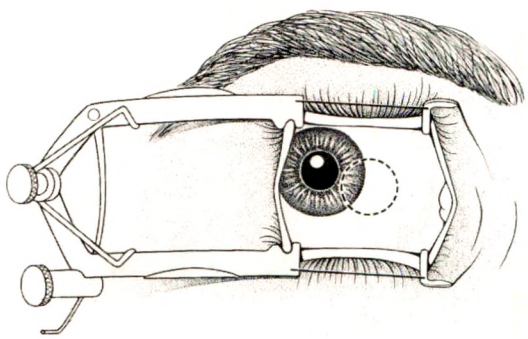


FIG. 1. Sketch illustrating the technique of Sr^{90} therapy. After local anesthesia, the eyelids are separated by a retractor. The patient is instructed to gaze laterally at the index finger held in proper position by the physician. The Sr^{90} applicator is placed on the limbus of the cornea where the head of pterygium was surgically resected. The dotted line represents the margin of the treatment field.

TABLE II

AGE INCIDENCE OF PTERYGIUM

Age Range	No. of Patients	Percentage
1 –10	0	0
11–20	1	1.6
21–30	14	22.5
31–40	16	26.0
41–50	16	26.0
51–60	6	9.7
61–70	8	12.9
71–80	1	1.6
Total	62	100.0

62 patients: 46 (59 per cent) in the right eye, and 32 (41 per cent) in the left eye. Sixteen of the 62 patients (26 per cent) had bilateral pterygia.

Of the 78 pterygia cases treated, 8 cases required a second surgical resection and postoperative Sr^{90} treatment. One case required a third excision and Sr^{90} therapy. The recurrence rate was calculated to be 10 per cent after the first course of treatment, and only 1.2 per cent after the second course of treatment. Two of the 8 recurrent cases were treated with a single dose of 2,000 reps. The interval between the completion of therapy to the appearance of the recurrence ranged from 2 months to 18 months (Table III).

By means of the naked eye and slit-lamp examinations, it was found that 21 eyes (27 per cent) developed telangiectasis in the treated conjunctiva; in 3 cases (4 per cent), a scar was found at the limbus where the head of the pterygium was resected. One patient, who had received Sr^{90} treatment with doses of 5,000 reps to each of 2 adjacent fields, showed keratitis. No radiation cataract was encountered in any of the treated eyes (Table IV).

There was a total of 124 scrapings of the conjunctiva on 124 eyes. Seventy-eight eyes were irradiated with the beta ray from Sr^{90}. The remaining 56 eyes, which had not received irradiation, were used for control. The length of time after Sr^{90} therapy ranged from 1 month to 11 years (Table V).

TABLE III

RECURRENCE OF PTERYGIUM AFTER BETA THERAPY

Case	Dose Received	Duration after Therapy
1	1,000 rep×3	2 months
2	1,000 rep×3	3 months
3	1,000 rep×3	10 months
4	1,000 rep×3	5 months
5	1,000 rep×3	16 months
6	1,000 rep×3	18 months
7	2,000 rep×1	8 months
8	2,000 rep×1	8 months
	2,000 rep×1 (2nd Rx)	5 years

Rx = treatment.

TABLE IV

COMPLICATIONS OF POSTOPERATIVE SR^{90} THERAPY FOR PTERYGIUM

Complications	No. of Cases	Per Cent of Total
A. *Conjunctiva*		
Telangiectasis	21	27
Scar formation	11	14
B. *Cornea*		
Scar formation	3	4
Keratitis	1	1.3
C. *Sclera*		
Atrophy	0	0
D. *Uvea*		
Iritis	0	0
Iris atrophy	0	0
E. *Lens*		
Radiation cataract	0	0

TABLE V

MATERIALS FOR CYTOLOGIC STUDY

Duration after Sr^{90} Therapy	No. of Eyes
1–6 months	18
7–12 months	4
1–2 years	34
3–4 years	11
5–6 years	2
7–8 years	5
9–10 years	3
11–12 years	2
Total	78



Fig. 2. High power photomicrograph of the exfoliative cells scraped from the untreated control eye showing normal conjunctival cells. The nuclei are uniform in size and shape. The chromatin is in a finely granular pattern. The nuclear membrane is smooth in outline. The cells are cuboid or square in shape. The cytoplasm is clear and transparent.

CYTOLOGIC FINDINGS

Control Group (Normal Cells). The structure of the exfoliative conjunctival epithelial cells in the control group was normal, as illustrated in Figure 2. The nuclei were round or oval shaped and were of uniform size. The chromatin showed a fine granular pattern. The nuclear membrane was smooth in outline. The cells were usually cuboid or square in shape and the boundaries between the cells were clearly defined. The transparent cytoplasm took a slightly blue stain.

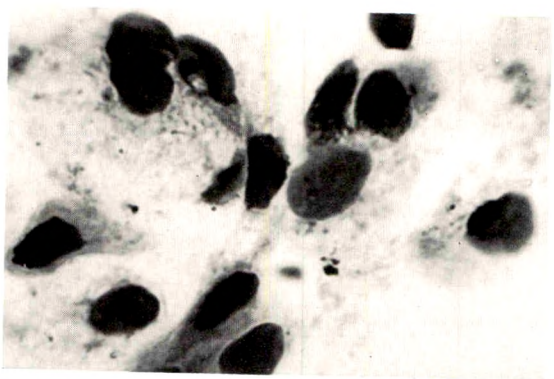


Fig. 3. High power photomicrograph of the exfoliative cells 3 years after receiving 3,000 reps from Sr^{90} therapy showing polymorphism of the nuclei. The size and shape of the nuclei are varied. The chromatin is coarser and darker. The margin of the nucleus is irregular.

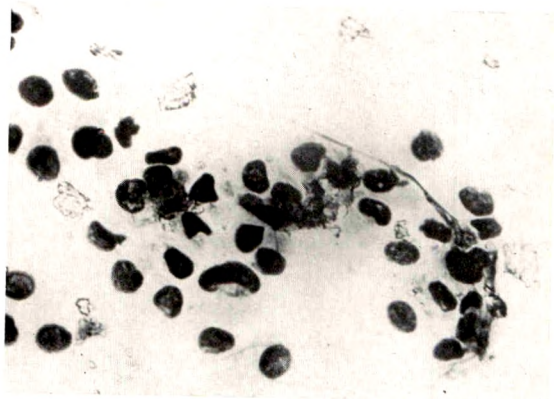


Fig. 4. Low power photomicrograph of exfoliative cells, 1 month after completion of 3,000 reps from Sr^{90} therapy showing the abnormal nuclei. Areas of absent chromatin staining are seen along the peripheral or central portion of the nucleus, producing either a crescentic or a clover-leaf defect. The polymorphism of the nuclei is again demonstrated.

Irradiated Group. Conjunctival epithelial cells, which had been subjected to beta radiation, showed alterations in the nucleus. The nuclei became irregular in size and shape, many assuming bizarre configurations (Fig. 3 and 4). The chromatin granules were hyperchromatic and coarse. Defects of chromatin along the peripheral or central portion of the nucleus, producing either crescentic or clover-leaf areas of diminished staining, were observed (Fig. 4 and 5). Striking nuclear enlargement was

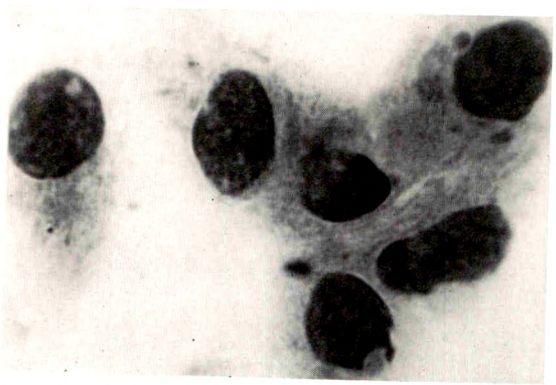


Fig. 5. High power photomicrograph of the exfoliative conjunctival cells 2 years after Sr^{90} therapy for a total dose of 3,000 reps, showing the defects of chromatin which are less severe than those 1 month after irradiation (Fig. 4).

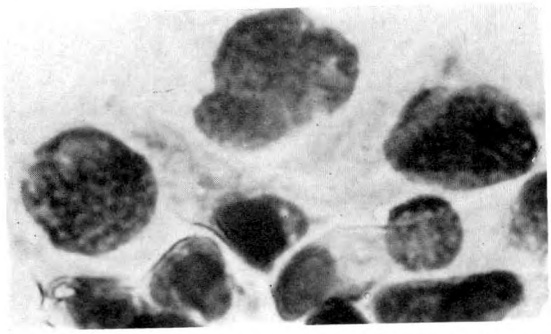


FIG. 6. High power photomicrograph of the exfoliative conjunctival cells 2 months after completion of 3,000 reps delivered by Sr^{90}, showing the appearance of giant cells in conjunction with the other abnormal nuclei. Defects of the chromatin are also noted.

occasionally seen (Fig. 6). The changes described were best demonstrated in those cells irradiated 1–6 months previously, while those irradiated 5–11 years ago showed less conspicuous changes.

The size and shape of the cytoplasm in the irradiated cells showed little departure from the normal. Many elliptical and spindle cells were seen in the conjunctival cells irradiated within 6 months.

DISCUSSION

The increasing use of beta radiation therapy in the treatment of benign ophthalmologic diseases, either postoperatively or by radiation therapy alone, points to the necessity of studying these radiation effects upon the treated cells.

Weekly doses of 1,000 reps for 3 treatments delivered by Sr^{90} radiation was found to be the optimum time dose for pterygium postoperatively. This therapy scheme yielded a control rate of 90 per cent without producing serious complications, including radiation cataract. The dose to the equator of the lens after 3,000 reps on the surface was calculated to be 150 reps, which is considered to be noncataractogenic. Abe,[1] who treated 50 pterygia with Sr^{90} postoperatively to a dose of 3,000 to 24,000 reps, found a relapse rate of 4 per cent. However, in 39 out of the 48 cured eyes, there developed an opacity in the lens equator as well as in the anterior and posterior subcapsular layers. Wilson[22] and others who treated pterygium at operation with a dose of 2,200 rads found no serious complications in their patients over a 5 year period; but, their recurrence rate was as high as 20 per cent. Lentino and associates[13] who analyzed 256 cases of pterygium treated by Sr^{90} with a dose of 5,000 reps in 2 weeks reported a recurrence rate of 3.6 per cent. However, there was no mention of lens complications in their report. The symptoms immediately following treatment were more severe. Fifty per cent of the treated eyes were reported to have developed telangiectasis.

Cytologic study of irradiated conjunctival cells disclosed distinct abnormalities in the nucleus. The changes, namely, polymorphism, giant cell formation and chromatin abnormalities are similar to those seen in cells irradiated by gamma or x-rays *in vivo* and *in vitro*.[3,11,12,17–19,21] These changes, although best demonstrated within 6 months, were observed as long as 5 years following beta irradiation. The severity of the changes varied in individuals, probably due to individual radiosensitivity. Despite the persistent cellular changes, no serious sequelae in the conjunctiva were observed up to 11 years. This is a preliminary study in the evaluation of the significance of the persistent abnormal changes of the cells after radiation therapy.

SUMMARY

Sixty-two patients with pterygium were treated by Sr^{90} postoperatively with doses of 1,000 reps weekly for 3 weeks and were evaluated by naked eye, slit-lamp, and cytologic examinations.

Complications from beta irradiation were mild. Ten per cent of the patients had recurrences of the pterygium 2 to 18 months after completion of the first course of the treatment. Only 1.2 per cent of the pterygia recurred after the second course of therapy.

Distinct cellular changes were observed in the irradiated conjunctiva. The changes were those of polymorphism, giant cell for-

mation and chromatin abnormalities.

Despite the persistent change of the cells, no serious sequelae in the conjunctiva were found as long as 11 years after radiation therapy.

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ROHRAD-AREA CURVES IN TREATMENT PLANNING*

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IT HAS been a common practice to administer an "air dose" of 100, 150, 200, etc., roentgens to each radiation treatment field and to construct treatment time charts corresponding to these exposures. The normal method of estimating tumor dose in rads includes the following steps: (1) read percentage depth dose from tables; (2) increase the air exposure rate by an appropriate backscatter factor according to the field size; (3) multiply Step 1 by Step 2 to obtain exposure rate at the tumor site; (4) multiply by treatment time; and (5) convert this exposure to rads by multiplying by the appropriate factor. ROHRAD-area curves (or tables) eliminate the need for repetitive calculations during a day's treatment schedule by incorporating these factors into depth dose tables.

The initials ROHRAD are used to clearly differentiate a table or graph of these values from normal depth dose tables and graphs. The initials arise from the words *R*ads per *O*ne *H*undred *R*oentgens *A*ir *D*ose. Although the term "air dose" is considered improper terminology[1] today, it was in common use at the time that the term ROHRAD was coined.[5]

CONVERSION OF DATA

The usual depth dose tables are converted into tables almost equivalent to ROHRAD tables when modified by the backscatter factor, the air exposure variation, and the rad-to-roentgens conversion factor. In order to complete the conversion, the tables must be adjusted to indicate rads at the given depth and field size in terms of 100 roentgens air exposure to a 10×10 cm. field and modified by 2 small factors, which will be discussed later.

The reference of all data to the 10×10 cm. field air exposure contributes much to the simplification in this concept, but is frequently a point of confusion when first introduced to the therapist. Figure 1, which illustrates the well recognized concept that the air exposure varies with field size, is normalized to represent the exposure rate of a 10×10 cm. field as 100 per cent. In the ROHRAD system, the 100 per cent air exposure for a 10×10 cm. field is selected as the standard reference point. To obtain the skin exposure for a selected field in terms of the standard field, the 100 per cent $D_{0.5}$ value of the depth dose table is modified by the backscatter factor and related to the standard field by the variation shown in Figure 1. Having established the factor relating the 0.5 cm. exposure value at a selected field to the standard field, any set of depth dose values may be modified by this factor to produce a table where each depth dose value is in terms of a per cent of the air exposure for the standard field.

Next, each of these values may be multiplied by 0.965 (for Co^{60} radiation) to convert the exposure in muscle to rads (absorbed dose). Conversion of all of the data of the depth dose table in this manner results in a chart showing rads at a desired depth (tumor) in terms of a per cent of the air exposure of the standard field.

Two additional minor modifications alluded to previously must be incorporated into the final data. Cobalt depth-dose charts refer to a 100 per cent number at the 0.5 cm. depth, whereas ROHRAD-area curves refer to a 100 per cent number at the surface. The surface number (air exposure) must be reduced by the inverse square law to obtain the correct exposure at the treatment skin-source distance plus 0.5 cm. Secondly, the primary beam is absorbed by 0.5 cm. of tissue, reducing the intensity at the 0.5 cm. depth and introducing another correction which must be applied.

Consider the following example:

* From the Radiology Department, Hackley Hospital, Muskegon, Michigan.

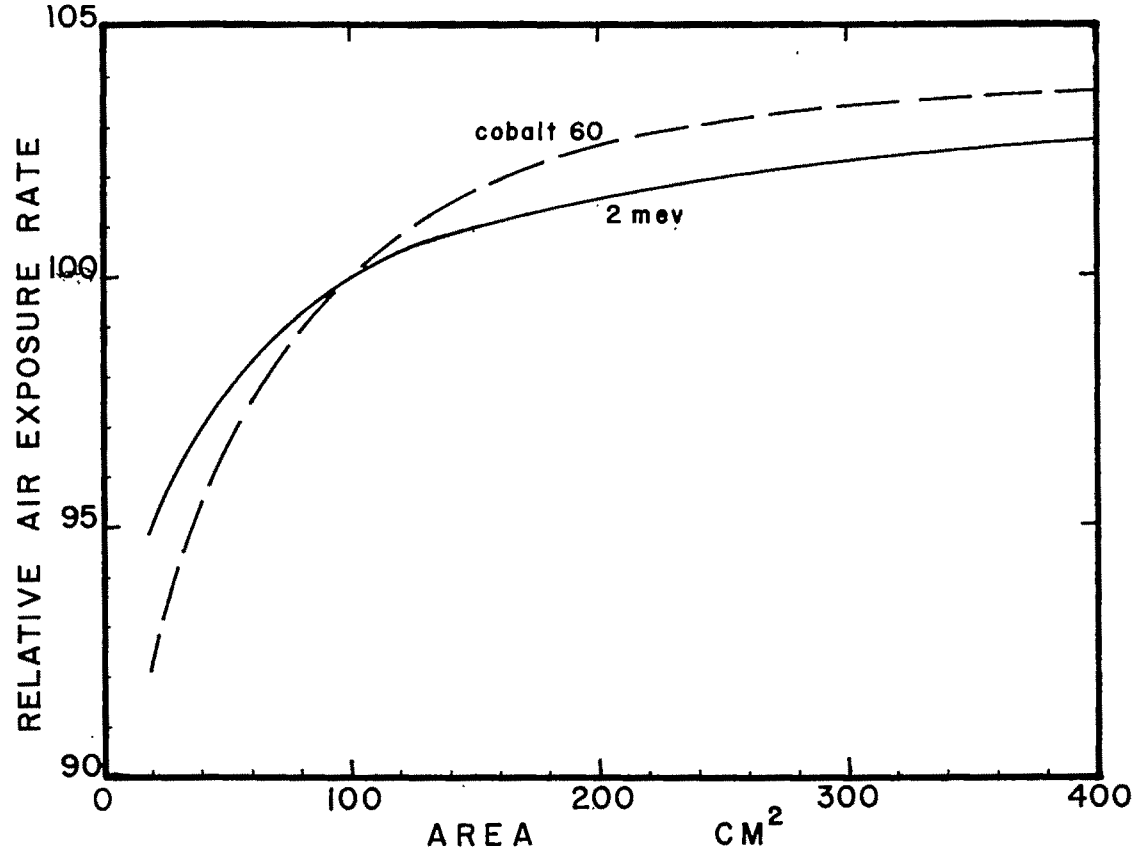


FIG. 1. Variation of air exposure rate with field size. The data of this graph represent the average of data obtained from several authors. The graphs have been normalized to read 100 at a field size of 10×10 cm.

Air exposure for 10×10 cm. field	100 per cent
To obtain the percentage relation of the absorbed dose at a 10 cm. depth for a 20 × 20 cm. field, multiply by the following factors	
Air exposure variation	1.036
Backscatter	1.045
Roentgens to rad conversion	0.965
Absorption and distance correction	0.97
Per cent depth dose (expressed as a fraction)	0.603
Over-all factor	61.1 per cent

The over-all factor would indicate that the tumor at a 10 cm. depth, when using a 20×20 cm. field, will receive 61.1 rads when the equipment is operated for the time period necessary to produce 100 roentgens air exposure to a 10×10 cm. field. This over-all factor has been given the name ROHRAD.

GRAPH CONSTRUCTION

Normal depth dose tables may be converted to ROHRAD tables by the application of a constant factor for each field size. The value of this conversion factor for each field size is shown in Figure 2. This graph was constructed by correlating the published values of several authors for the variation of air exposure, backscatter, or the two combined and then finding average.[2,3,6–11] These results were then modified by the roentgen-to-rad conversion and absorption-distance correction factors.

Finally, the application of this conversion factor to the data of Table B-18 in *The Physics of Radiology*[7] results in Table I; and Table B-15 of this same textbook was used to construct Table II. Subsequent plotting of the data of Tables I and II pro-

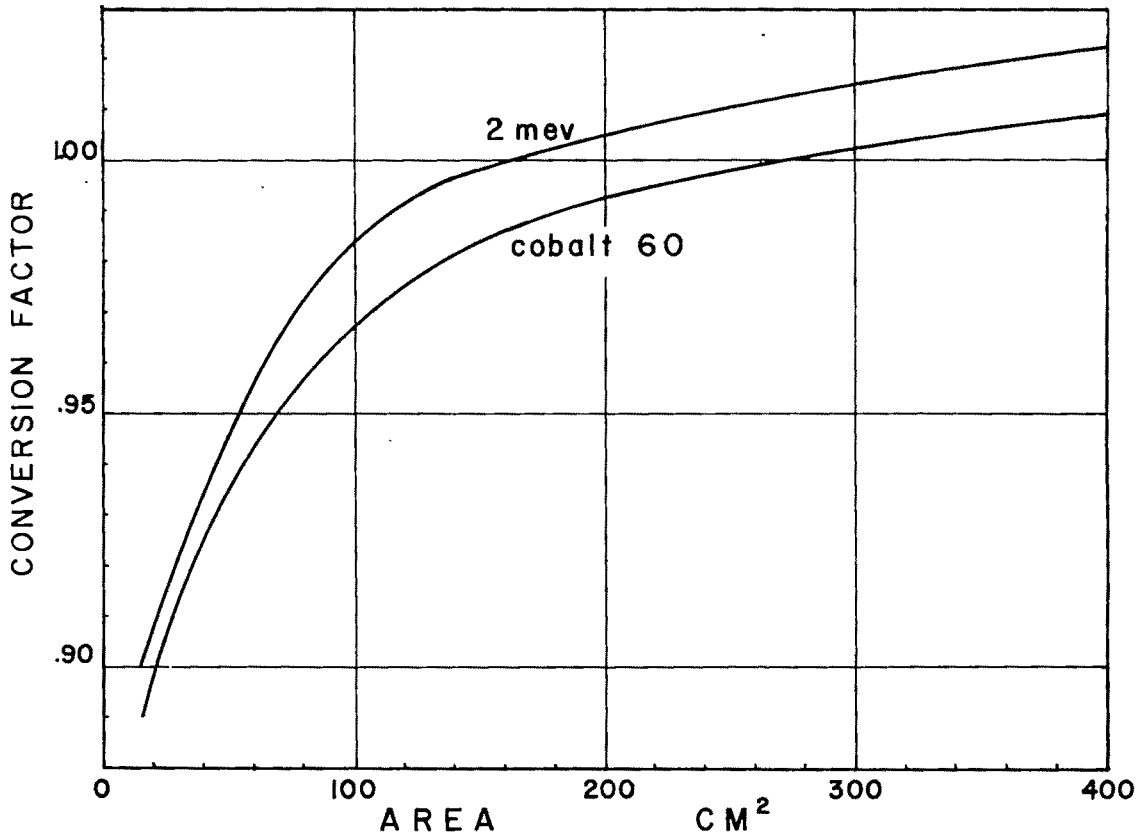


FIG. 2. ROHRAD conversion factor. Depth dose tables may be converted to ROHRAD tables by the application of these conversion factors. These values are not specific for a given piece of equipment; they are average values obtained from several sources.

vided sufficient points to construct Figures 3 and 4 as illustrated.

APPLICATION

When using the ROHRAD system, the therapist selects the desired tumor dose, adjusting the skin or air exposure to accommodate the selected tumor dose. Thus, a prime advantage of this system is apparent in the fact that the tumor dose is the primary parameter and the skin exposure is a secondary parameter.

To calculate treatment time, the following equation is used:

$$T=\frac{100\,D}{HI}, \qquad (1)$$

where T = treatment time in minutes, D = selected tumor dose in rads, H = ROHRADS at tumor depth, I = equipment output or air exposure rate for a 10×10 cm. field, 100 = the constant 100 which arises from the fact that H is expressed in rads per 100 roentgens.

Although D may have any value chosen by the therapist, a common convenient number is 200 rads and in all subsequent formulas and examples the value 200 is substituted for D. To make calculations using a different tumor dose, simply substitute the desired value for 200.

For treatments of two or more fields per day, the treatment time for each field may be calculated by adding the ROHRADS before calculating the treatment time as determined by Equation 1. This procedure produces an equal skin exposure for each field, although the contribution of each field to the total tumor dose may be different.

The skin dose, which would be the dose at 0.5 cm. depth for cobalt and 2 mev. radiation, may be calculated in either of the following manners:

$$\text{Skin dose (rads)} = 0.01\ TI\ H_{0.5}, \qquad (2)$$

where T = treatment time, $H_{0.5}$ = the ROHRAD value for the 0.5 cm. depth, and I = equipment air exposure rate for a 10×10 cm. field.

$$\text{Skin dose (rads)} = \frac{H_{0.5}\ 200}{H_T}, \qquad (3)$$

where $H_{0.5}$ = the ROHRAD value for the 0.5 cm. depth, and H_T = the total ROHRAD value for the tumor depth.

The correct depth dose or ROHRAD for other than circular or square fields should be obtained from the area equivalent of the elongated field. Observe in Table III that the ROHRADS for a 6×20 cm. field are found by reading the graph along the 74 cm. area line rather than along the 120 cm. line.

TABLE I

ROHRAD—AREA TABLE

Cobalt 60 — Source-skin Distance 80 cm.

Depth (cm.)	Area of Field in Square Centimeters				
	20	50	100	200	400
0.5	89.6	93.5	96.6	99.2	100.9
1	86.9	91.3	94.9	97.6	99.4
2	81.5	86.5	90.2	93.0	94.8
3	76.4	81.5	85.4	88.3	90.4
4	71.3	76.7	80.6	83.7	86.0
5	66.4	71.9	75.8	79.3	81.5
6	61.7	67.1	71.2	74.6	77.1
7	57.2	62.5	66.6	70.1	72.4
8	52.8	58.1	62.0	65.8	68.6
9	48.7	53.8	57.8	61.6	64.7
10	44.9	49.8	53.8	57.6	60.8
11	41.4	46.2	50.0	53.9	57.2
12	38.2	42.8	46.6	50.4	53.8
13	35.2	39.6	43.4	47.2	50.6
14	32.5	36.7	40.4	44.1	47.5
15	30.0	34.0	37.6	41.5	44.7
16	27.8	31.6	35.0	38.7	42.1
17	25.7	29.3	32.7	36.2	39.6
18	23.7	27.1	30.3	33.9	37.2
19	22.0	25.2	28.3	31.4	35.0
20	20.2	23.4	26.4	29.8	33.0

TABLE II

ROHRAD—AREA TABLE

2 mev. — Half-value Layer 7.6 mm. Pb — Target-skin Distance 100 cm.

Depth (cm.)	Area of Field in Square Centimeters				
	20	50	100	200	400
0.5	90.8	94.6	98.4	100.5	102.2
1	87.4	92.0	96.4	99.0	100.7
2	83.0	88.6	92.9	95.7	97.7
3	77.0	84.1	87.9	91.6	94.1
4	72.3	78.9	83.7	87.4	90.3
5	67.3	73.9	78.8	82.6	85.1
6	62.6	68.6	73.6	77.2	80.3
7	57.9	63.4	68.2	72.0	75.3
8	53.6	57.8	62.7	67.2	71.0
9	48.9	54.7	59.7	63.4	66.6
10	45.0	50.6	55.7	59.3	63.1
11	41.4	46.1	51.6	54.9	57.3
12	37.9	43.2	47.6	51.3	55.0
13	35.0	39.8	44.3	47.6	51.6
14	32.3	36.9	41.2	44.8	48.2
15	29.8	34.0	38.1	41.8	45.4
18	23.4	27.2	30.7	34.2	37.5
20	19.2	22.5	25.6	29.1	32.1

APPLICATION EXAMPLES

SINGLE FIELDS

Calculate the time to administer a tumor dose of 200 rads and find the skin dose.

Given: Field size—12×12 cm.
Tumor depth—6 cm.
ROHRADS—73 (Co^{60})
Output—78.4 roentgens per minute to a 10×10 cm. field.

Equation 1 gives treatment time.

$$\text{Time} = \frac{100 \times 200}{73 \times 78.4} = 3.84 \text{ minutes.}$$

Equation 2 gives skin dose.

$$\text{Skin dose} = 0.01 \times 3.49 \times 95.7 \times 78.4 = 262 \text{ rads.}$$

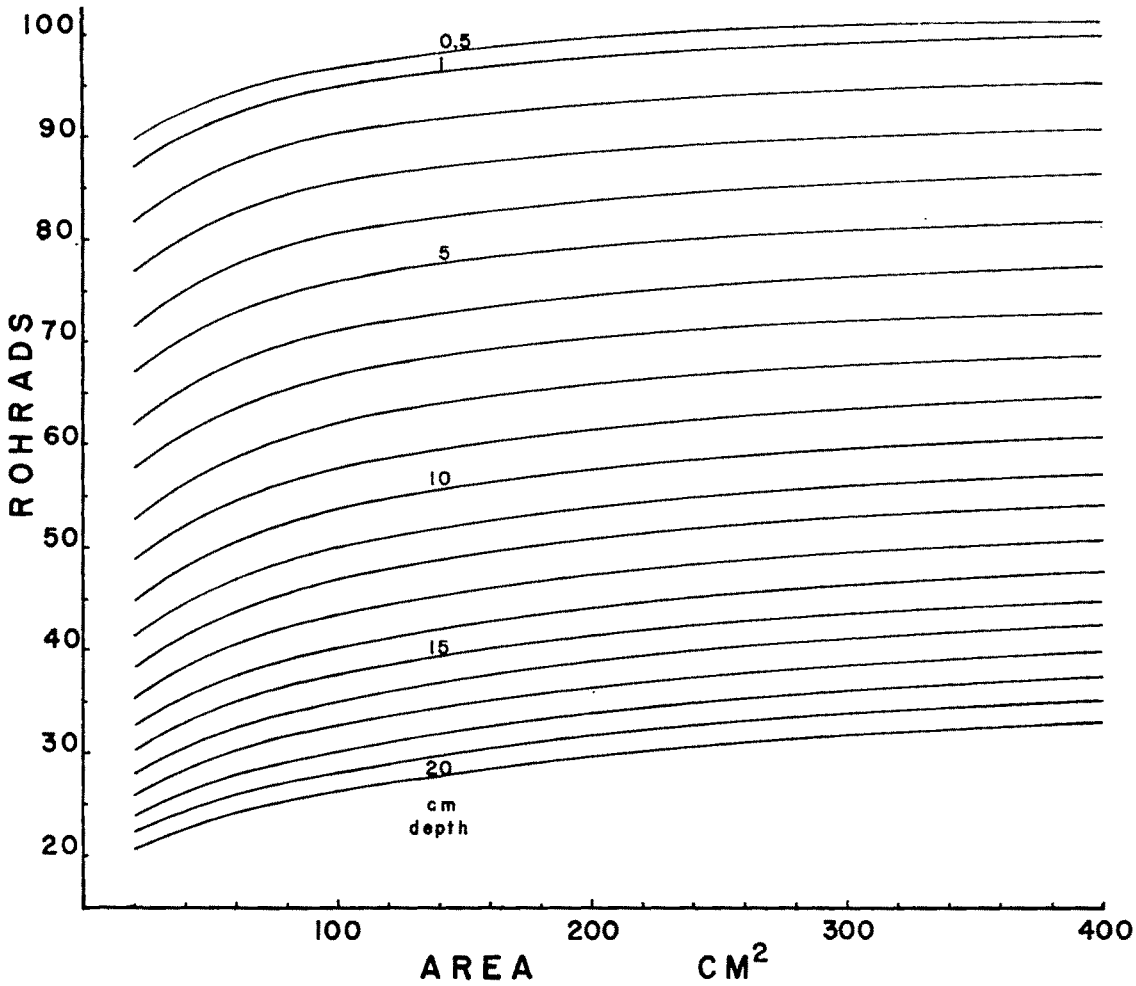


FIG. 3. ROHRAD-area curves for a cobalt 60 unit used at a source-skin distance of 80 cm. Application of the conversion factor of Figure 2 to a specific depth dose table (see text for details) produces this graph.

Equation 3 may be used also.

$$\text{Skin dose} = \frac{95.7 \times 200}{73} = 262 \text{ rads.}$$

MULTIPLE FIELDS

Calculate the treatment time to each of 3 fields and find the skin dose to each when the calculated tumor dose is 200 rads.

Given: Output—78.4 roentgens per minute.

2 lateral oblique fields—11×11 cm. tumor depth—12 cm. ROHRADS—48 (Co^{60}).

1 anterior field—15×11 cm.—tumor depth—8 cm. ROHRADS—64.5(Co^{60}).

First add the ROHRADS

$$H_T = 48 + 48 + 64.5 = 160.5.$$

Use Equation 1 to calculate treatment time.

$$\text{Time} = \frac{100 \times 200}{160.5 \times 78.4} = 1.59 \text{ minutes.}$$

The treatment time is 1.59 minutes *to each field.* Use Equation 2 to calculate the skin dose.

$$\text{Skin dose} = 0.01 \times 1.59 \times 97.5 \times 78.4$$
$$= 122 \text{ rads to each field.}$$

$H_{0.5}$ for an 11×11 cm. field has been used to calculate the skin dose in this example, but the third field is 11×15 cm. If the skin

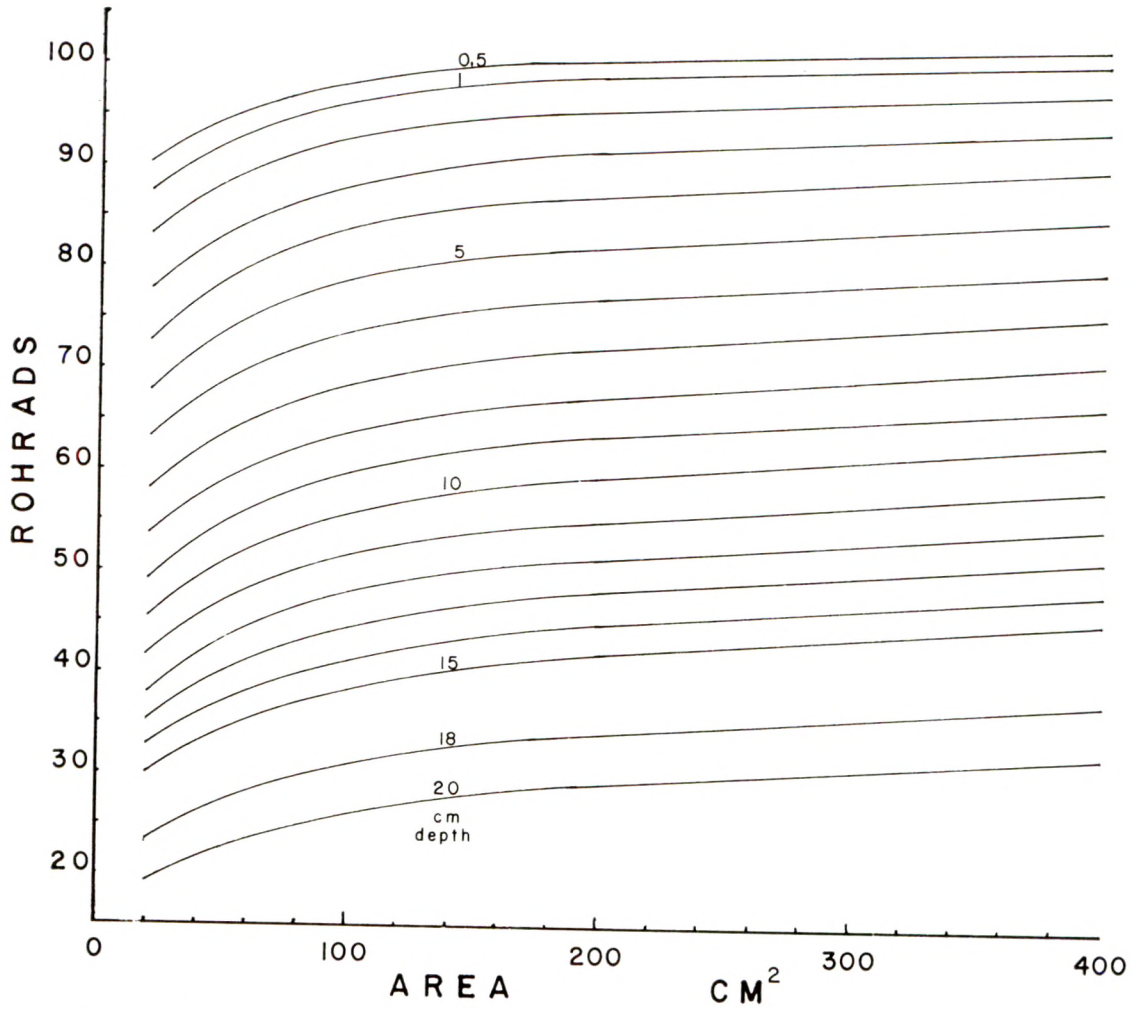


Fig. 4. ROHRAD-area curves for a 2 mev. unit used at a target-skin distance of 100 cm. Application of the conversion factor of Figure 2 to a specific depth dose table (see text for details) produces this graph.

dose value of 122 rads per field is used, what error occurs in the statement of the skin dose for the 11×15 cm. field? Figure 2 shows $H_{0.5}$ to be 97.5 for the 11×11 cm. field and 98.5 for the 11×15 cm. field. It is obvious, then, that the difference in skin dosage to these 2 fields is actually less than 2 rads. If the therapist will accept an error of less than 2 per cent in the statement of skin dose, only one calculation is necessary for the 3 fields.

NONUNIFORM TREATMENT SCHEDULE

If the therapist prefers to treat each of 3 fields in sequence on subsequent days, the proper treatment time for the above examples is not 1.59 minutes. Notice in this example that the total treatment time each day when treating 3 fields is 1.59+1.59+1.59 or 4.77 minutes. If only 1 field is being treated each day, the total treatment time to that field must be 4.77 minutes. Each of the other fields will be treated for 4.77 minutes on subsequent days. The skin dose to the field being treated is:

$$\text{Skin dose} = 0.01 \times 4.77 \times 97.5 \times 78.4 = 365 \text{ rads.}$$

Each skin field, of course, receives this dose every third day. The actual tumor dose per

Table III

Area equivalence of elongated fields*

For other than circular or square fields use the equivalent area given in this table for reading the ROHRAD-area curves. For simplicity, the area values have been rounded off to the nearest 5 units for fields above 10×10 cm.

Dimensions in cm.	2	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	22
4	8																		
5	9	20																	
6	10	23	29																
7	11	27	34	41															
8	12	30	38	47	55														
9	12	32	42	52	62	71													
10	13	33	45	56	68	79	89												
11	13	34	47	59	72	85	97	110											
12	14	35	48	62	76	91	103	115	130										
13	14	36	50	65	80	95	109	125	140	155									
14	14	37	52	67	83	99	114	130	150	165	180								
15	15	38	53	68	85	102	118	135	155	170	190	205							
16	15	39	54	70	88	106	134	140	160	180	195	215	235						
17	15	39	55	71	90	108	126	145	165	185	205	225	245	260					
18	15	40	56	72	92	111	130	150	170	195	215	235	255	270	295				
19	16	40	57	73	93	113	134	155	175	200	220	245	265	285	310	330			
20	16	41	58	74	95	115	138	160	180	205	230	255	275	300	320	345	375		
22	16	41	59	76	97	118	142	165	190	215	240	265	290	320	345	370	395	420	
24	16	42	60	77	99	121	146	170	195	220	250	275	305	335	365	395	420	445	500

* The basic data of "A Note on the Calculation of Dose in X-ray Fields," by Day[4] were expanded and modified in form to construct this table. According to Johns,[7] Day's data are applicable to cobalt 60 radiation even though they were originally written for a beam quality of 1.8 mm. Cu half-value layer.

day will not be 200 rads; but it will total 600 rads in 3 days. The exact weighted division of the total dose is in the ratio of the ROHRADS for that field to the total ROHRADS.

Tumor dose on Day 1

$$= \frac{H_{12}\,600}{H_T} = \frac{48 \times 600}{160.5} = 179.$$

While the tumor dose for the other oblique field will be 179 rads, the same calculation shows the tumor dose from the anterior field to be 242 rads.

Comment

When treating 3 fields per day for a total tumor dose of 200 rads, it is convenient to write the tumor dose as 200/3 for each field. This shorthand is intended to convey the message that the tumor dose for a given field is part of the total dose of 200 rads which is accumulated from the treatment of 3 fields on that day. It does not indicate that the field contributes exactly 1/3 of the total tumor dose of 200 rads. The therapist wishing to state the exact tumor dose for a given field must calculate it from Equation 1.

When a standardized daily tumor dose is established, it is convenient to eliminate repetitious calculations by constructing a treatment time table of the form shown below. For cobalt 60 units it is necessary to reconstruct this table each month or every 2 months; for electrical units recalculation of the chart is only required at the time of a change in the output of the equipment. Only 1 Table is required because the ROHRAD system is based on the calibrated air exposure for a 10×10 cm. field; no other air exposure rate is needed to complete this treatment chart.

Isodose curves in terms of iso-ROHRAD lines

Additional convenience is obtained when the Department's isodose curves are written in terms of iso-ROHRAD lines. To obtain this, the normal isodose curves are

TREATMENT TIME REQUIRED TO GIVE 200 RADS

Use this chart during June 1968

Cobalt Unit No. 2
Output 80.4 r/min.

ROHRADS	Minutes	ROHRADS	Minutes	ROHRADS	Minutes
40	6.22	90	2.76	140	1.78
41	6.07	91	2.73	141	1.76
42	5.92	92	2.70	142	1.75
.	.	.	.	.	.
.	.	.	.	.	.

re-plotted to show iso-ROHRAD lines. Summation of intersecting points of the iso-ROHRAD curves which have been superimposed according to the treatment plan produces ROHRAD values at miscellaneous points in the treatment area. Additional points that may be needed to adequately describe a complete iso-ROHRAD line may be obtained by interpolation. The completed plot is a group of iso-ROHRAD sums. As shown previously, this is the parameter needed when using multiple fields. The therapist selects the iso-ROHRAD sum line encompassing the tumor volume and inserts its value into Equation 1 for H to calculate the treatment time.

In a further refinement, the ROHRAD system has been used at Hackley Hospital for the past 7 years to set a treatment exposure meter rather than to calculate treatment time. Our General Electric 2 mev. x-ray generator contains an ionization chamber which discontinues the treatment at a given total exposure setting. This system is superior to a timer setting on this equipment because there is a 10 to 15 second build-up of the x-ray beam at the start of the treatment, and this relatively long, variable build-up period would produce excessive variations in total treatment when the treatment time varies between 1 and 4 minutes. The ionization chamber of this meter is placed between the target and the shutters causing its output to be independent of field size. The ROHRAD system with its incorporation of field size variations is thus ideal for use with this treatment exposure meter.

DISCUSSION

The ROHRAD information of Tables 1 and 11 and Figures 3 and 4 is based on the averages of data available in the literature. These data are not necessarily correct for any particular piece of equipment. Probably the main source of difference between these results and any one piece of equipment will arise in the area of the air exposure variation with field size. It has been shown that air exposure variation with field size (Fig. 1) is dependent upon the collimators, source size, etc., of the equipment.

In the calculation of treatment time for multiple fields, it is assumed that the therapist prefers to administer equal skin doses. If this assumption is not applicable, the calculations for multiple fields do not apply and the therapist must treat each field separately, calculating each dose according to Equation 1.

It has been suggested by a colleague that this system would be ideal for use with a betatron unit, where the air exposure rate varies daily.

CONCLUSION

In external beam radiation therapy procedures, the determination of central axis tumor doses or isodose curves in rads requires several calculations on numbers secured from depth dose tables or graphs. These repetitious calculations can be eliminated by incorporating them into graphic

or tabular presentation of depth dose data. Further simplification occurs by using an air exposure of 100 roentgens to a 10×10 cm. field as a reference point. The number obtained subsequent to these calculations has been given the name ROHRAD. ROHRAD-area curves (or tables) greatly simplify the calculation of central axis tumor doses in rads, reduce the occurrence of calculation errors, and simplify calibration chart construction for cobalt units.

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THE DIAGNOSTIC PROBLEMS OF ISOLATED, CIRCUMSCRIBED BREAST TUMORS

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ISOLATED, circumscribed cancers of the breast offer the greatest diagnostic difficulties to the roentgenologist. Their close resemblance to benign lesions such as fibroadenomata and cysts is usually the basis for these difficulties.

Since early, accurate diagnosis of breast cancer is so vital to therapy and prognosis, the radiologist must become familiar with both the clinical and pathologic manifestations of this disease. They are varied, insidious, and may fall into several classifications. The classifications are far from satisfactory, reflecting for the most part the descriptive and conventional arrangements of the various pathologists who have formulated them.

The following classifications of cancers represent a good working plan based on roentgen findings: (1) spiculated masses; (2) circumscribed masses; (3) distorted structural patterns due to cancer; (4) microcalcifications with any of the above patterns; and (5) secondary signs due to lymphatic spread, edema, or other inflammatory reactions. The diagnostic terminology of the radiologist must then be reconciled with the individualistic terminology of the pathologist.

Probably 90 per cent of all breast cancers are ductal in origin and will be papillary, comedo, scirrhous, medullary, or colloid in type. Of these, the roentgenologist will identify most easily many of the infiltrating duct cancers with scirrhous formations. But the smoothly contoured scirrhous cancers, the medullary and the colloid cancers are more difficult to assess, and it is the purpose of this report to point out some diagnostic criteria which help to distinguish these circumscribed cancers from fibroadenomata and cysts, which they frequently resemble.[1,3–5,7]

DIAGNOSTIC SIGNS

In order to gain some impression of the incidence and diagnostic signs connected with these isolated, circumscribed tumors, we reviewed a series of 112 consecutive cases of which 68 were found to be cancers. The remainder were either cysts or fibroadenomata. Of the cancers, 57 were scirrhous of the infiltrating duct varieties, 4 were medullary, and the rest were variously designated as adenocarcinoma, carcinoma simplex, large-cell carcinoma, and infiltrating papillary carcinoma.

Twenty-one of the scirrhous cancers were easily identified by their characteristic radiating striae or strands. Of the remaining 36 cancers, an incorrect diagnosis of cyst or fibroadenoma was made in 7. The other 29 cancers were correctly designated, either as outright cancers or as lesions warranting biopsy without delay because malignancy was suspected. Of the 44 benign lesions diagnosed as either cysts or fibroadenomata, 4 were cancers (Table 1).

Infiltrating duct carcinomas with productive fibrosis—the so-called scirrhous carcinomas—probably comprise 70 per cent of all forms of breast cancer. The desmoplasia and productive fibrosis are what give these tumors their characteristic gross and roentgenographic appearance. While some of these tumors are rounded, the majority tend to be oval, ellipsoid, or discoid in contour. When the characteristic dendritic strands and striae radiating from

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TABLE I

DIAGNOSTIC ROENTGEN CRITERIA OF 112 ISOLATED, CIRCUMSCRIBED BREAST TUMORS

Type of Tumor	No.	Radiating Strands	Circumscribed	Notched	Comet-tail Extensions	Microcalcifications	Secondary Signs	Incorrect Diagnoses
Scirrhous cancer	57	21	31	7	6	20	26	5
Medullary cancer	4	0	4	4	0	1	1	0
Miscellaneous cancers	7	1	1	1	1		1	2
Cysts	29							1
Fibroadenomata	15							3
Total	112							

their irregular margins are visible, their roentgen recognition becomes easy (Fig. 1).

About 60 per cent of these scirrhous cancers are circumscribed, with no perifocal reaction or so slight a reaction as to escape roentgen detection. Such lesions may appear benign and resemble the medullary types of cancer more than the scirrhous variety. Recognition of the edematous disturbance of the perifocal trabecular architecture requires careful scrutiny (Fig. 2). Occasionally a group of ducts or vessels may be stretched or tugged into an unusual alignment, or there may be actual disruption of the adjacent glandular structures (Fig. 3).

In the more rapidly progressive types, an edematous reaction may take place in the surrounding tissues, which will blur the component structures. Associated vascular engorgement might be discerned, and the perifocal edema might extend into the neighboring skin, which can be detected as thickened on the roentgenogram, even though it often may not be appreciated clinically. This perifocal edema probably accounts for the fact that the clinical measurements of these lesions exceed those derived from the roentgenogram (Fig. 4).

About 35 per cent of these tumors have associated microcalcifications by the time they are discovered. The curious, punctate, crystalline-like calcium deposits which may be noted on the roentgenogram are sometimes located within the tumor, but they can also be found elsewhere in the breast. Finding these deposits on the roentgenogram requires proper exposure and meticulous searching. The films should preferably be overexposed and viewed with increased illumination and a magnifying glass. The minuteness of some of these deposits may elude the naked eye. Because the final diagnosis can be reliably placed on the finding of these calcifications, no matter what other diagnostic ambiguities exist, a search for them becomes exceedingly important[2] (Fig. 5).

Medullary cancers with lymphoid infiltration comprise about 5 per cent of all cancers. They are sufficiently distinctive to warrant a separate classification, not only from the viewpoint of the pathologist but also from that of the roentgenologist. Because these tumors are circumscribed, the initial tendency is to confuse them with benign cysts and fibroadenomata on the roentgenogram.[1,5] However, their nodular or globoid appearance is not the result of encapsulation, and careful scrutiny of the circumscribing margins will reveal wavy, sinuous, undulating or angular contours which in one or more places will lead off to a comet tail-like extension of fibrosis into the perifocal parenchyma (Fig. 6; 7; and 8).

When these tumors are first seen, they may be no larger than 3 cm. to 6 cm. in diameter, and their clinical dimensions are usually greater than those measured on the roentgenogram. These tumors tend to be less aggressively malignant than those of

the infiltrating duct varieties. One of the unusual characteristics of these tumors is the abundant perifocal infiltration of small lymphocytes. Hemorrhagic and anemic necroses are common findings, especially in the larger tumors, which may fungate and resemble inflamed cysts (Fig. 9).

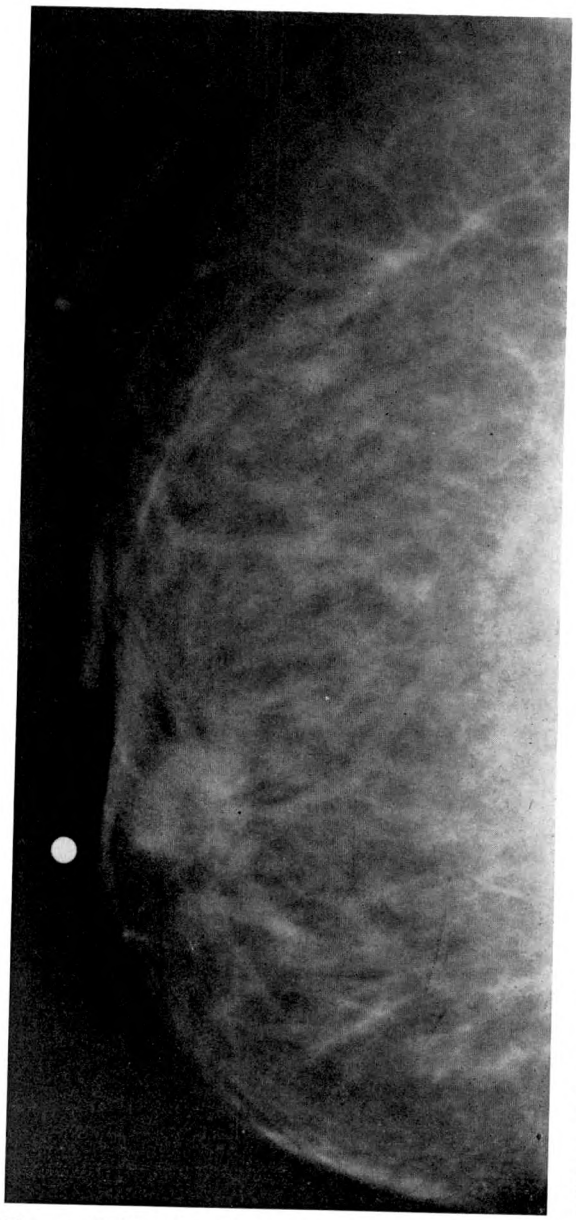


Fig. 1. Infiltrating duct cancer with scirrhus. A nodular cancer with radiating striae resembling a scirrhus was palpated as a benign lesion by the patient's physician. The perifocal edema blurs structural details and accounts for the thickening of the adjacent skin.

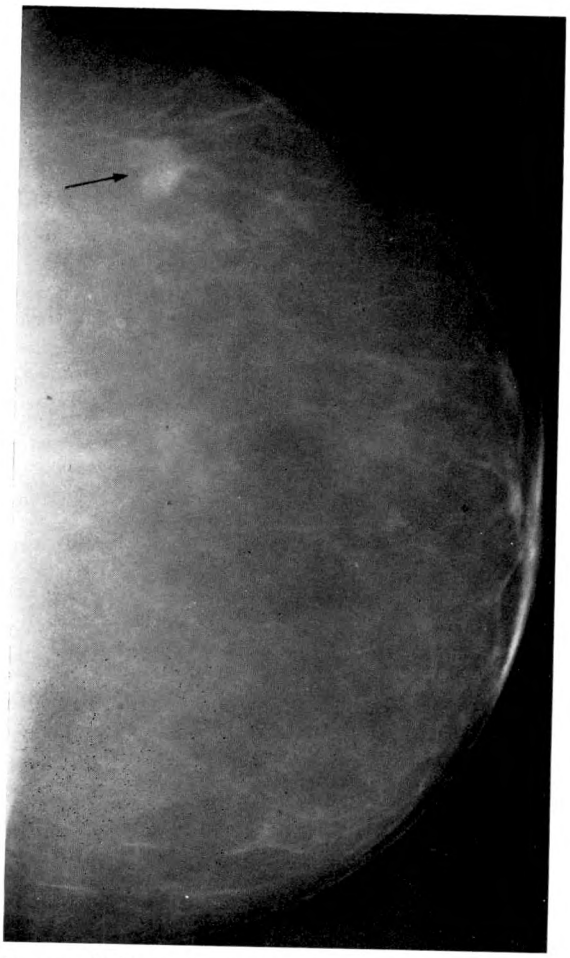


Fig. 2. Infiltrating duct cancer with scirrhus. An isolated, circumscribed, notched lesion (arrow) suggests cancer. A movable, painless mass about 1.5 cm. in diameter was palpable in the breast of a 58 year old woman. The mass measured only 8 mm. in diameter on the roentgenogram. The striae extending to the area of thickened skin stand out due to edema.

It becomes obvious, therefore, that all circumscribed tumors must be carefully examined by the radiologist. An isolated, circumscribed lesion, even though only a few millimeters in diameter, which is found in a woman over 35 years of age, should raise a suspicion of possible malignancy. If the margins of such tumors are wavy, undulating, or lack the sharp, smooth contours of a benign process; if a tongue-like projection of fibrosis leads away from any portion of the margin; or if blurring of

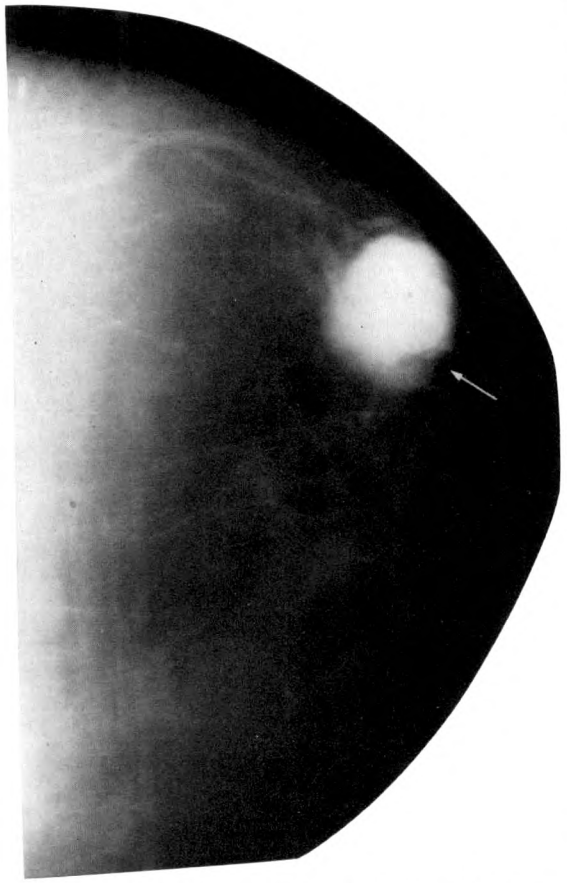


FIG. 3. Infiltrating papillary carcinoma. A circumscribed tumor with smooth margins and notching (arrow). The adjacent trabeculae and vessels are stretched and disaligned.

the perifocal tissues due to edema is present, sometimes with other secondary signs such as vascular engorgement and thickening of the skin, the suspicion of malignancy should be verified or ruled out by biopsy (Fig. 10). The roentgenologist may not find it easy to convince the surgeon to operate, since many of these tumors present misleading physical signs of a benign process.

DISCUSSION

The occurrence of notches among isolated, circumscribed cancers of the breast is a helpful diagnostic sign. These notch-like defects have also been described in malignant nodules of the lungs by Rigler.[8] We do not wish to imply that notching is pathognomonic of cancer, but when the interpreter of the roentgenogram is in considerable doubt about the differential diagnosis, the presence of a notch-like defect in the circumscribed margin of the lesion may sway his judgment to cancer, and in many cases he will be right.

Care must be exercised in differentiating these notches from those that may be the result of superimposition of blood vessels, adjacent fibrous structures, the recesses between the lobulations of a bosselated fibroadenoma, or the angled notching due to superimposed clusters of cysts.

The reasons for the occurrence of notching in these circumscribed tumors are not

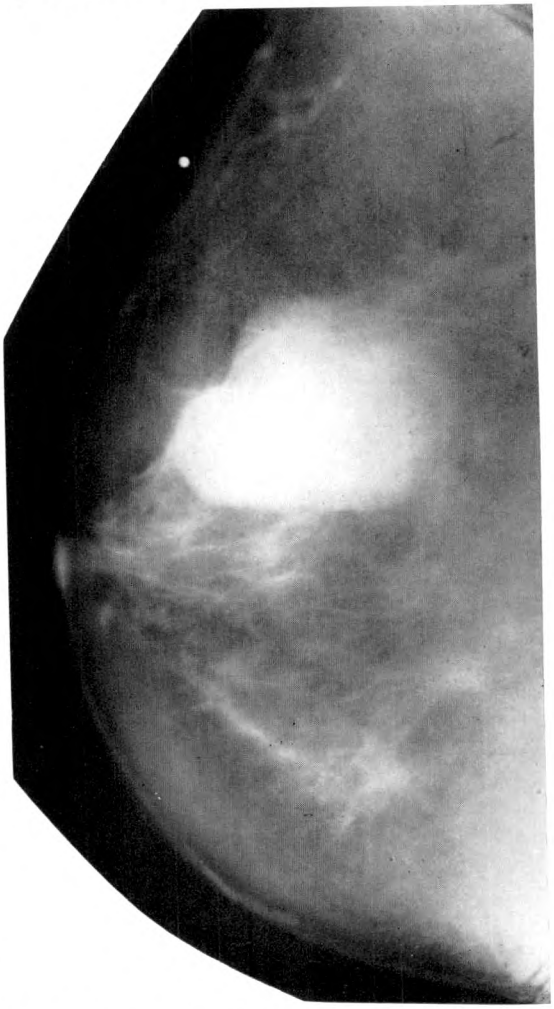


FIG. 4. Infiltrating duct cancer with scirrhus. A notched, smoothly contoured, isolated mass with surrounding edema suggested cancer to the radiologist rather than a cyst or fibroadenoma, which this lesion resembles.

clear. One of the possibilities that might be considered is the pseudo-hilum which might form around the most nutrient blood vessel supplying the tumor. But a more probable explanation is merely the uneven contraction of the perifocal pseudofibrous capsule which forms around these slow-growing tumors with which most pathologists are familiar.

When these solitary, circumscribed tumors lack all the primary and secondary signs of malignancy and only the presence of notching suggests the possibility of cancer, they must be differentiated from cysts and fibroadenomata.[5,6]

CYSTS

When single cysts reach large enough proportions to crowd available space, they may become quite hard and tense. On palpation, they may be freely movable and fluctuation may be detected. On roentgenograms, their walls are usually smooth and sharply defined, and in fatty breasts they can easily be seen on the roentgenogram, sometimes even when they are not palpable clinically.

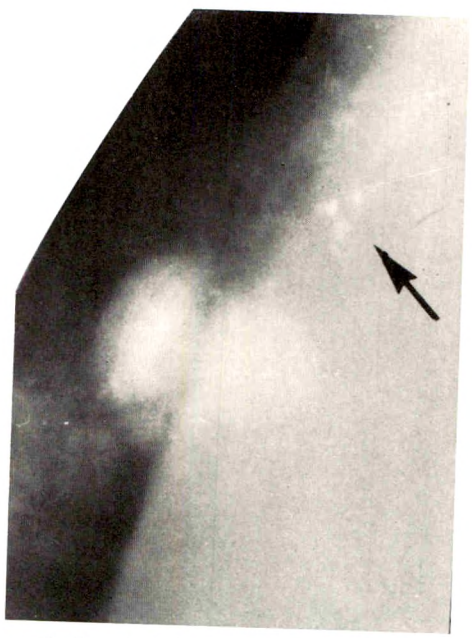


FIG. 5. Infiltrating duct carcinoma with scirrhus. The isolated, irregularly notched mass with an aggregate of microcalcifications deposited nearby (arrow) suggested the diagnosis of cancer.



FIG. 6. Medullary cancer. The undulating, notched contours of this cancer resemble the bosselations of a fibroadenoma. A small fibroadenoma is located nearby with a flake of calcium on its surface. (The dense spherical body nearby is the skin marker placed over the palpable mass.)

The roentgen diagnosis of cysts is not usually difficult, except when they become inflamed, either from trauma or infection. The question of cancer then arises. If a cyst is multilocular, or if there are several cysts partially superimposed each upon the other, a notch-like defect might be seen simulating that which can occur in circumscribed cancers (Fig. 11).

The epithelium lining of most cysts is so degenerated that it is usually beyond stimulation by factors which induce neoplasia. Still, it is not always possible to be sure that a large cyst does not contain carcinoma. In addition, the roentgenologist should always be alert to the possibility of a cancer occurring in a multicystic breast. Moreover, cancer may be found in an area remote from a palpable mass, and should be searched for in all cystic breasts.

It is our policy always to suggest complete removal of solitary cysts, unless the



FIG. 7. Medullary cancer. The undulating, slightly notched contours of this isolated mass suggested cancer rather than a fibroadenoma or a cyst, which it resembles.

surgeon permits us to re-examine an aspirated cyst after he has inflated it with air. We agree with Gros[6] that air should be introduced into the cyst after evacuation in order to show the presence of intracystic papillomata or cancer. If these lesions are present, they can then be visualized.

FIBROADENOMATA

It is possible that a single, discrete, movable and apparently circumscribed mass to which the skin is not adherent, found in a young woman, may be an early cancer of the most malignant type. But the greater likelihood is that the lesion is a benign fibroadenoma.[3] Discrete, smooth-walled lesions in mazoplastic breasts, especially in women under 25 years of age, are almost universally benign. But if the woman is 40 years of age and older, and an isolated, discrete lesion with sharply delineated margins is found, even in the absence of the notch sign, its removal for histopathologic examination is foresighted.

We no longer attempt to differentiate cysts from fibroadenomata merely from their roentgen appearance. Many fibroadenomata which have been present for a long time and have reached a large size are likely to become cystic. Many fibroadenomata are bosselated and the indentations thus produced can resemble the notching of a cancer. This often makes differential diagnosis of cancer very difficult (Fig. 12).

Rarely, a cluster of fibroadenomata may be superimposed, and the pseudo-notching so caused can resemble the notching of a cancer and make diagnosis a problem. With the development of various forms of plaque-like calcifications in fibroadenomata, however, their identification be-

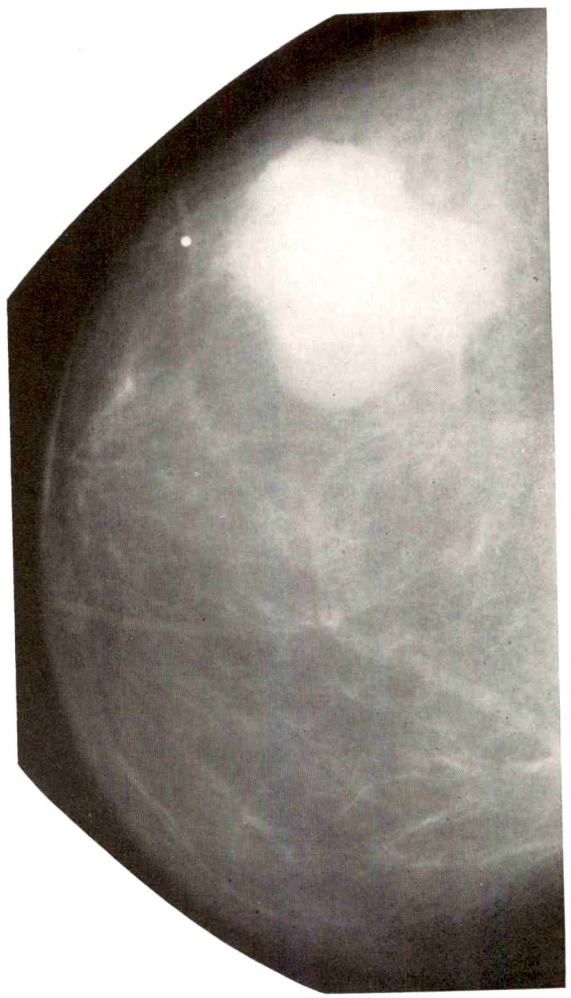


FIG. 8. Medullary cancer. The sinuous, undulating, angular contours of this isolated mass suggested cancer rather than a benign lesion.

comes easier and the therapeutic recommendations can become more positive.

SUMMARY

Probably 60 per cent of all breast cancers seen on roentgenograms are circumscribed, lacking the easily identifiable radiating striae and strands issuing from the periphery that are seen in scirrhous cancers. Since these circumscribed cancers are difficult to distinguish from benign lesions like fibroadenomata and cysts which they resemble, it is important that the roentgenologist pay strict attention to some of the secondary diagnostic signs.

Among these is the curious tendency for these tumors to have notch-like deformities in their outlines or comet tail-like extensions of one or more portions of their periphery, with progressive intensity of perifocal edema associated with vascular turgescence and thickening of the skin as the tumor enlarges. About 35 per cent of these tumors are associated with the presence of microcalcifications within or about them, and it is these secondary signs which are of great help in distinguishing such tumors from bosselated fibroadenomata, clusters of cysts, or multilocular cysts, which are

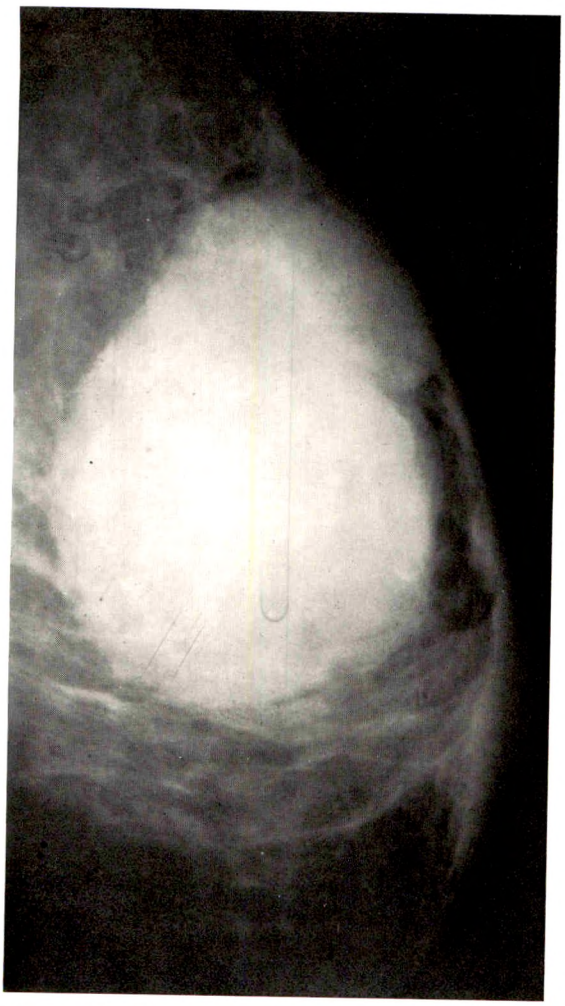


Fig. 9. Medullary cancer. These cancers may grow slowly and reach a large size before being discovered by the patient. Their smooth outlines, often notched, may mimic the appearance of inflamed cysts or bosselated fibroadenomata. Perifocal edema involves the skin.



Fig. 10. Infiltrating duct cancer with scirrhus. A palpable, movable mass was thought to be benign, but immediate biopsy was suggested by the roentgenologist because of the comet tail-like extension visible at the site of the spherical skin marker.

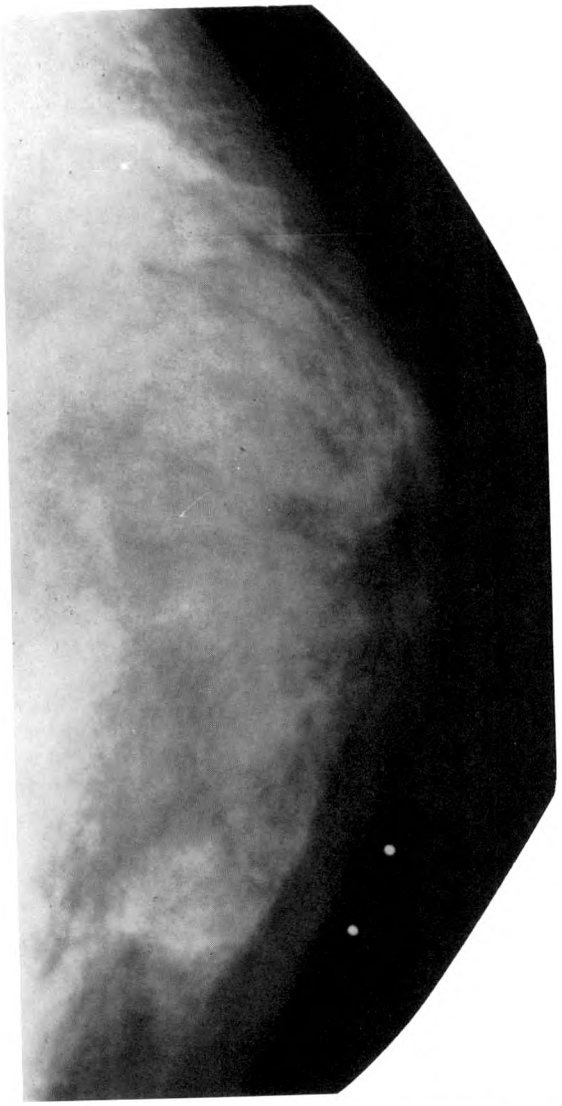


FIG. 11. A cluster of small superimposed cysts, the outlines of which appear as an undulating, notched margin resembling a cancer, which was the favored roentgen diagnosis. The tumor was palpable at the site of the skin markers and the clinician correctly suspected the presence of a benign lesion.

also characterized by angular notching of their margins.

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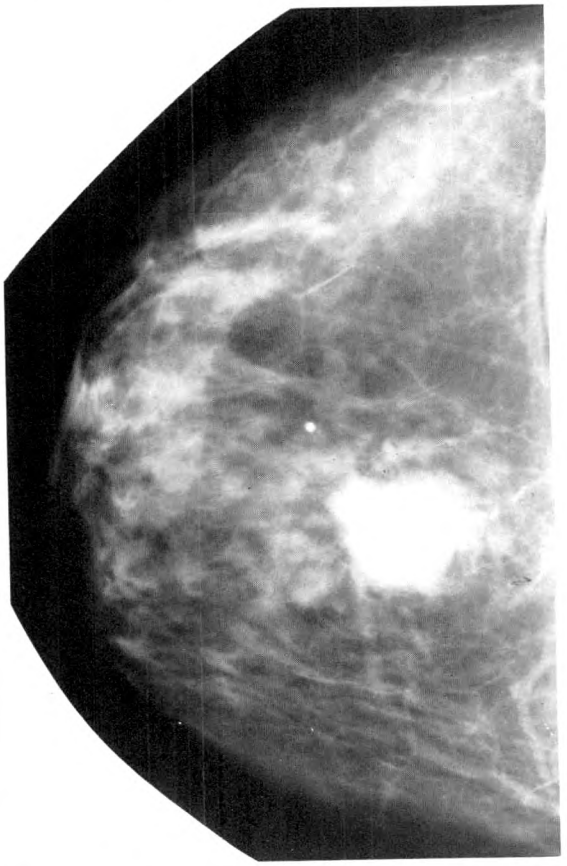


FIG. 12. Papilloma which resembles a notched, circumscribed cancer.

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A TV SYSTEM FOR DATA BLENDING AND CONTRAST ENHANCEMENT OF SCINTISCANS*

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IN ORDER to obtain optimum scintiscans with commercially available equipment, it may be necessary to rescan a given organ several times. However, this procedure yields control settings which do not necessarily produce optimum scans on other patients. Futhermore, considerations of patient comfort and equipment utilization preclude routine rescanning. Previous approaches to this problem include techniques [1,2] that are limited in versatility and do not permit both data blending and contrast enhancement. This laboratory has developed a TV system that permits rapid data blending, contrast enhancement and image reversal of the original scintiscan. Improved displays of scintiscans are obtained by simple adjustment of controls.

DESCRIPTION OF THE SYSTEM

The essential components of the system are shown in Figure 1. Lamps placed in front of the scintiphoto provide the necessary reflected light for the TV camera when a print (Polaroid) is being observed. A conventional viewing box, represented by the rear lamp, provides illumination when the scintiphoto is a film or transparency. The composite video signal from the TV camera is processed in the TV monitor in the usual fashion. A phase inverter, shown in the block below the TV camera, permits changing the polarity of the video signal. This allows one to reverse the black and white areas of the image appearing on the monitor. Brightness and contrast of the image can be altered by

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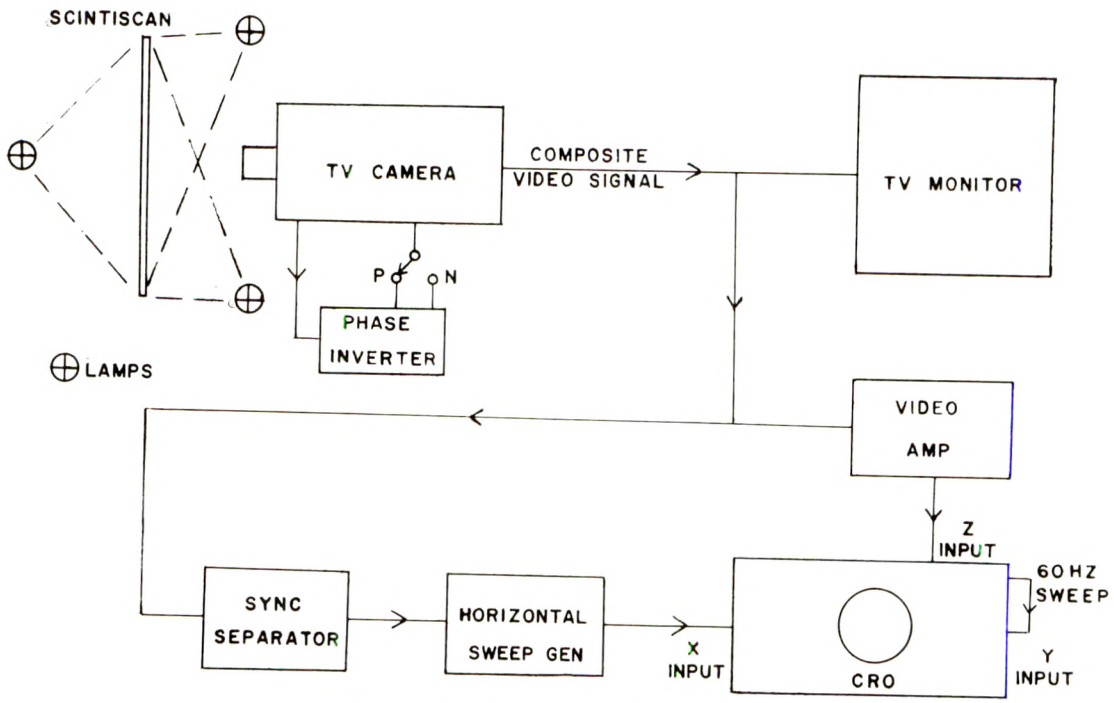


FIG. 1. Block diagram of TV system.

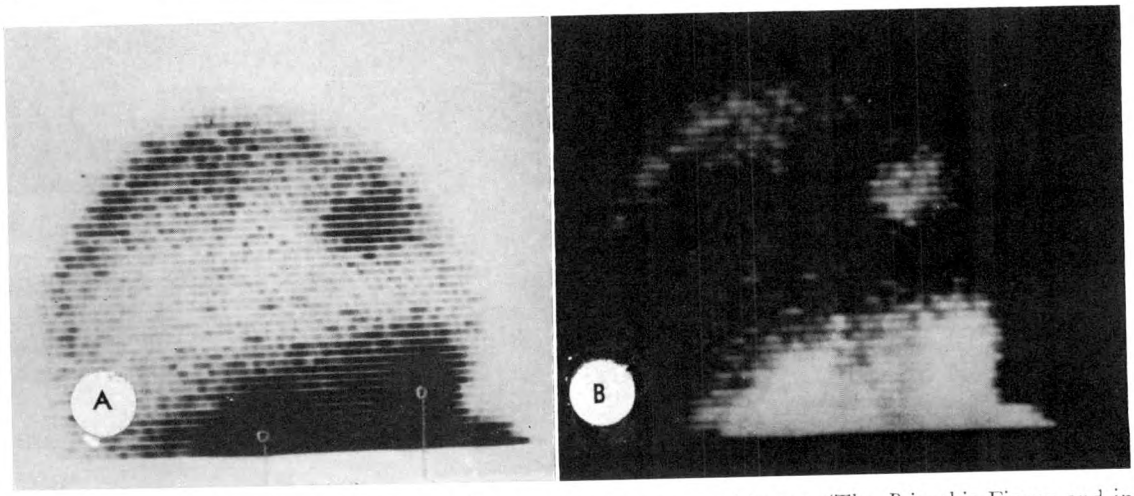


Fig. 2. (*A*) Original rectilinear scan, and (*B*) corresponding reversed image. (The *B* in this Figure and in Figure 3*B* refers to reversed image of rectilinear scan.)

varying the appropriate controls on the monitor.

For greater versatility the image of the scan is also displayed on a cathode ray oscilloscope (CRO). As shown in Figure 1 the composite video signal is also fed into a sync separator and video amplifier. The sync separator selects the horizontal pulses from the composite signal. These pulses are then used to synchronize the frequency of the horizontal sweep generator with that of the TV camera. The vertical sweep is derived from the sweep generator of the CRO and fed into its Y input. This sweep is synchronized with the line frequency (60 Hz) as is the vertical sweep in the TV camera. Therefore, it is unnecessary to recover vertical sync pulses from the composite video signal in order to accomplish vertical sweep synchronization. These horizontal and vertical sweeps produce the desired raster. The signal from the video amplifier, which provides a voltage gain of about 40, is fed into the Z input of the CRO. Variations in intensity of the cathode ray beam due to this amplified video signal

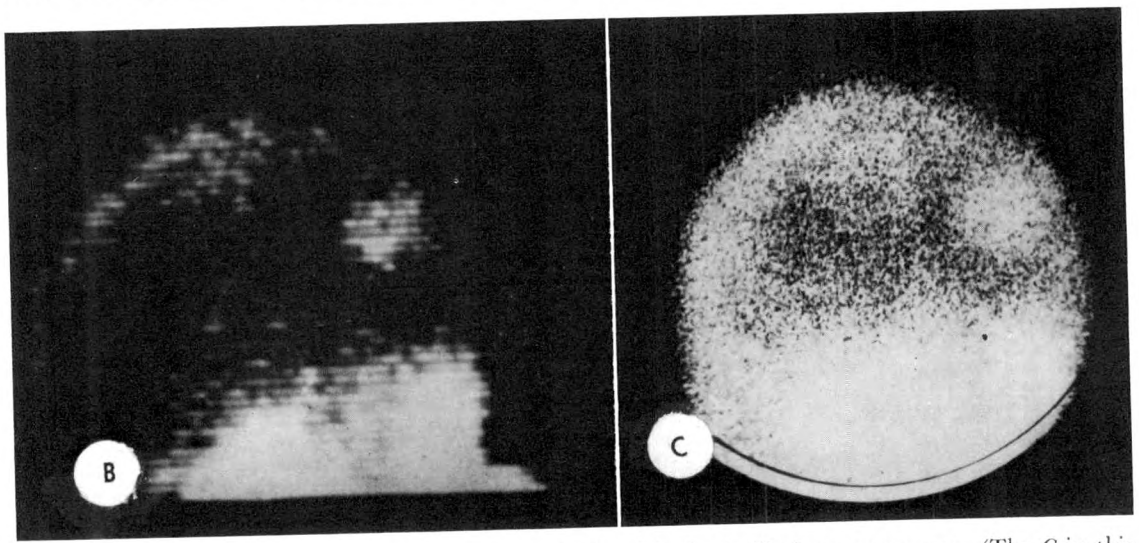


Fig. 3. (*B*) Reversed image of rectilinear scan, and (*C*) original scintillation camera scan. (The *C* in this Figure and in Figure 4*C* refers to original scintillation camera scan.)

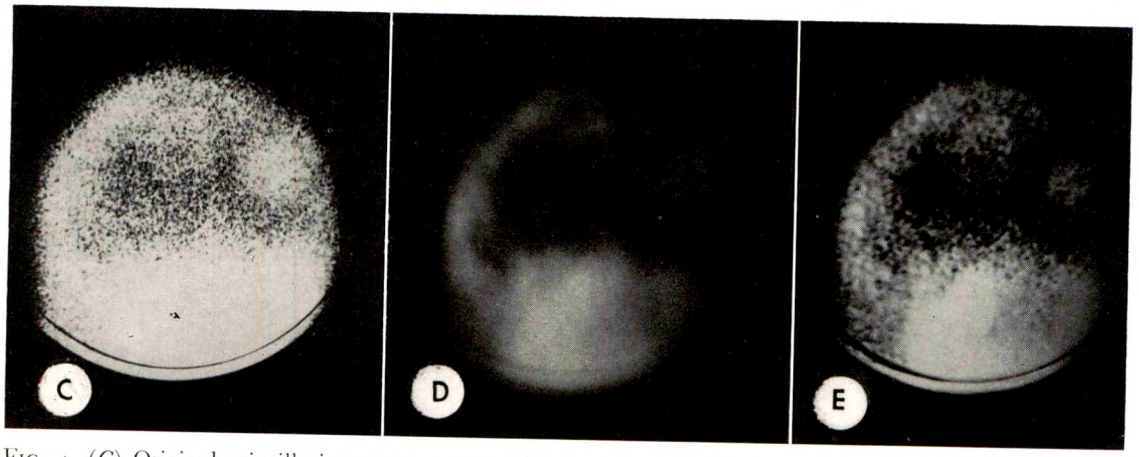


Fig. 4. (*C*) Original scintillation camera scan, (*D*) data-blended scan, and (*E*) contrast-enhanced scan.

produce the image on the phosphor. A cathode ray tube with a P_4 phosphor is used so as to yield a black and white image.

By reversing the polarity of the sweep voltage applied to the horizontal plates of the CRO a mirror image is obtained. This feature is useful for obtaining a direct photograph from those types of oscilloscope cameras which produce a mirror image.

Image brightness is varied by the beam intensity control on the CRO. Contrast enhancement is obtained by changing video amplifier gain and by varying the aperture on TV camera lens. The focus control on the CRO permits data blending.

To illustrate the versatility of the system, a brain scan of a patient was made with a rectilinear scanner and a scintillation camera. The original rectilinear scan is shown in Figure 2*A*. By changing the polarity of the video signal, the black and white areas are reversed (Fig. 2*B*). This image reversal feature permits a direct comparison of the displays from the two types of scanners as shown in Figure 3, *B* and *C*.

The original camera scan (Fig. 4*C*) is modified by the focus control producing the data-blended scan (Fig. 4*D*). The contrast enhancement shown in Figure 4*E* was obtained by varying the over-all gain of the system.

The use of photographic methods to obtain similar results would consume considerable time and effort.

CONCLUSION

The advantage of this TV system is that it allows the clinician to rapidly obtain the optimum image of the original scan by simple adjustment of controls.

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USES OF DESK COMPUTERS IN NUCLEAR MEDICINE*

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MANY tests performed daily in the Nuclear Medicine Laboratory involve fitting a single exponential function to a number of observed data points in order to determine such parameters as decay constants, half times of disappearance, and activity at zero time. Since these curves are logarithmic, they are usually drawn by plotting the observed data on semilogarithmic graph paper and then fitting to the points what appears to be the best straight line. This procedure is subjective and may be misleading, especially when there is considerable scatter of the data points. This gives rise to the possibility that different individuals may draw significantly different lines through the points.

As an alternative, the method of "least squares," or "regression analysis," which provides an objective method of determining the line of best fit, is suggested. If these calculations are done by hand, they are generally too time consuming for routine clinical procedures. The use of computers has been suggested but they are expensive for small groups such as a Nuclear Medicine Department. Small programmable desk calculators (such as the Olivetti Programma 101) whose programs can be externally stored on magnetic cards were tested and found satisfactory for obtaining the results required in this type of work.

A review of the method of regression analysis upon which this program is based is necessary to better comprehend how the calculators obtain the desired results.

As an example, consider in Figure 1 the following data points through which we wish to draw the line of best fit. We will define the line of best fit to be the line which

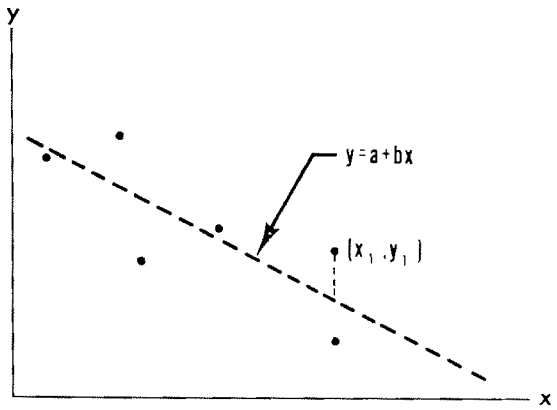


FIG. 1. Tentative line of best fit for the given points.

minimizes the sum of the vertical deviations between the data points and the line. These deviations will be squared to eliminate problems with sign, hence the name, method of "least squares."

The term we wish to minimize, therefore, is the sum of the deviations squared:

$$\Sigma(\text{dev})^2=\Sigma(y_i-y')^2=\Sigma(y_i-a-bx_i)^2$$

where y' is the point on the line which we have not yet defined, and y_i is the observed data point.

The constants to be determined are: a (the intercept of the line with the y axis) and b (the slope of the line). Consider what happens to $\Sigma(\text{dev})^2$ as we allow b to vary at will, leaving a fixed (Fig. 2).

Obviously, the $\Sigma(\text{dev})^2$ is going to be a minimum only for the line which is the best fit for the points (Fig. 2, arrow). A plot of $\Sigma(\text{dev})^2$ as a function of slope b, is demonstrated in Figure 3.

An expression of the slope of the curve in Figure 3 is found by taking the partial de-

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rivative of the term $\Sigma(\text{dev})^2$ with respect to b:

$$\frac{d\Sigma\,(\text{dev})^2}{db}=\frac{d}{db}\Sigma^i(y_i-a-bx_i)^2$$
$$=2\Sigma^i(y_i-a-bx_i)(-x_i).$$

An exactly analogous argument holds for a:

$$\frac{d\Sigma\,(\text{dev})^2}{da}=\frac{d}{da}\Sigma^i(y_i-a-bx_i)^2$$
$$=2\Sigma^i(y_i-a-bx_i)(-i).$$

By setting these expressions equal to zero (zero slope is a horizontal line) and solving simultaneously for a and b, we find the point on the plane ab directly below the bottom of the 3 dimensional cup in Figure 4, or mathematically:

$$o=2\Sigma^i(Y_i-a-bx_i)(-x_i)=\Sigma x_iY_i-a\Sigma x_i-b\Sigma x_i^2$$
$$o=2\Sigma^i(Y_i-a-bx_i)(-1)=\Sigma Y_i-na-b\Sigma x_i$$

Rewriting: $a\Sigma^ix_i+b\Sigma^ix_i^2=\Sigma^ix_iY_i$

$$an+b\Sigma^ix_i=\Sigma^iY_i$$

and solving simultaneously for a and b:

$$a=\frac{\begin{matrix}\Sigma^ix_iY_i & \Sigma^ix_i^2\\ \Sigma^iY_i & \Sigma^ix_i\end{matrix}}{\begin{matrix}\Sigma^ix_i & \Sigma^ix_i^2\\ n & \Sigma^ix_i\end{matrix}}=\frac{(\Sigma^ix_iY_i)(\Sigma^ix_i)-(\Sigma^ix_i^2)(\Sigma^iY_i)}{(\Sigma^ix_i)^2-n\Sigma^ix_i^2}$$

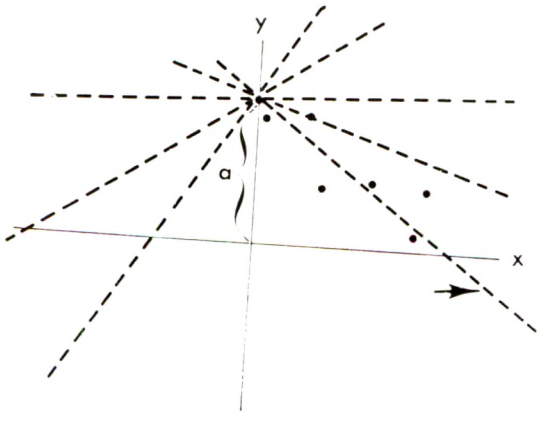


Fig. 2. Slope of line is allowed to vary at will, while the "zero" point is kept fixed.

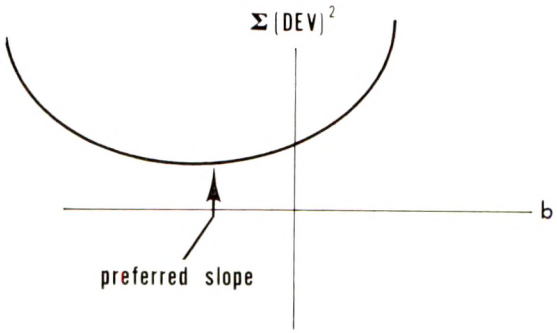


Fig. 3. Plot of $\Sigma(\text{dev})^2$ as a function of slope.

$$b=\frac{\begin{matrix}\Sigma^ix_i & \Sigma^ix_iY_i\\ n & \Sigma^iY_i\end{matrix}}{\begin{matrix}\Sigma^ix_i & \Sigma^ix_i^2\\ n & \Sigma^ix_i\end{matrix}}=\frac{(\Sigma^ix_i)(\Sigma^iY_i)-n\Sigma^ix_iY_i}{(\Sigma^ix_i)^2-n\Sigma^ix_i^2}.$$

We have now completely defined the line $y=a+bx$ which best fits the points.

In the present problem, of course, we are working with the equation:

$$A=A_0e-\lambda t.$$

Taking the natural logarithm on both sides: $\ln A=\ln A_0-\lambda t$ which we see is exactly the same as saying $y=a+bx$, where $b=-\lambda$. Substituting:

$$a=\ln A_0=\frac{[\Sigma(t\cdot\ln A)](\Sigma t)-[\Sigma(t)^2](\Sigma\ln A)}{(\Sigma t)^2-n\Sigma(t)^2}$$

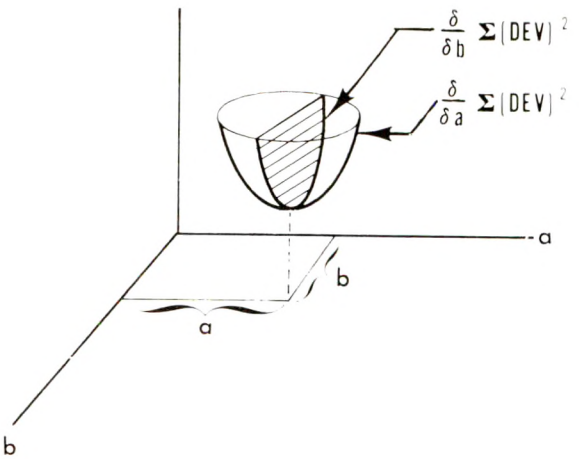


Fig. 4. Graphic expression of the slope of the line.

$$b = -\lambda = \frac{(\Sigma t)(\Sigma \ln A) - n\Sigma(t \cdot \ln A)}{(\Sigma t)^2 - n\Sigma(t)^2}.$$

While for the purpose of finding the half life we would need to calculate only lambda ($T\frac{1}{2} = 0.6932(\lambda) - 1$), $\ln A_0$ is also needed to give an estimate of the experimental error.

To find the standard deviation around the half life, we first plot the 68 per cent confidence bands around the regression line using the standard formula for deviation around a mean:

$$\text{S.D.} = \sqrt{\frac{\Sigma(Y_i - y')^2}{n-1}}.$$

In this case, of course, y' is not a constant but is the function of x_i just defined ($y' = a + bx_i$) and must be calculated for each point. Since this standard deviation is calculated for the y axis (counts) we must divide our result by lambda to find the standard deviation around the half life, which is on the x axis.

METHOD

To illustrate the importance of this method of obtaining the results required in these types of analysis, we have analyzed 37 red blood cell survival studies.

In these studies we followed a standard procedure to perform the tests, and the half times were determined both by plotting the data on semi-logarithmic graph paper and using the programmable calculator.

Determination of half times by regression analysis also can be performed without a programmable calculator or computer and is equally accurate but includes more chance for error and takes much longer.

RESULTS

In our studies we compared results obtained when the data are plotted on semi-logarithmic graph paper with the results obtained using the "least squares" method and the programmable calculator.

Table I illustrates that the results compare favorably in most of the cases. In some other cases we found surprising discrepancies. Differences of half life span of the red blood cells were up to 30 per cent. Standard deviation calculated by computation ranged from ±3 to ±5.5 days. Some studies were reported as being normal while they were probably abnormal, others were reported as abnormal half life spans while they were probably normal (Table II). In these cases the standard deviations were high (over ±3 days) and the difference found between results obtained by plotting the data on semi-logarithmic graph paper and obtaining the half time of disappearance by computation were always larger than two standard deviations.

There were some very peculiar cases,

TABLE I

RESULTS OBTAINED BY COMPUTATION COMPARE FAVORABLY WITH RESULTS OBTAINED BY PLOTTING THE DATA

Half Life for Red Blood Cell*

Graph Data	Computed Data	Difference	Standard Deviation
31	31	0.0	0.48
14	15	1.0	1.02
25	24	1.0	1.44
19	20	1.0	1.28
35	35	0.0	0.75
20	22	2.0	1.10
27	26	1.0	1.35
18	17	1.0	0.80
27	26	1.0	1.10
17	16	1.0	0.55
21	22	1.0	0.93
24	23	1.0	0.64
25	24	1.0	0.75
32	33	1.0	0.96
19	18	1.0	0.36
20	20	0.0	0.31
20	20	0.0	0.60
27	26	1.0	0.82
14	15	1.0	1.47
16	15	1.0	0.63
22	21	1.0	0.68
30	30	0.0	1.71
25	24	1.0	1.84
35	35	0.0	0.54
20	20	0.0	0.64
10	9	1.0	0.90
16	16	0.0	1.05
32	33	1.0	0.96

* Figures shown are in days.

such as the one illustrated in Figure 5, in which an error of plotting led to a very confusing result. Two points, for 14 and 17 days, were incorrectly plotted. The operator drew a presumably correct line which resulted in a half life value of 25 days. For this particular case, the result obtained by computation using the true values was 40 days, with a standard deviation of ±4.5 days.

Since the difference between these results was greater than two standard deviations, it is likely that there is a significant difference between the two results. In addition, the standard deviation using the computer was large, which in itself suggested technical errors and/or poor quality control and reproducibility. In this case the operator could have reviewed the results for any error in technique or method.

CONCLUSION AND SUMMARY

Thirty-seven red blood cell survival tests were studied using both regression analysis by computation and plotting on semi-logarithmic graph paper.

In 78 per cent of the cases both methods compare favorably. In this group of cases, the plotted result was within two standard deviations of the calculated result.

TABLE II

8 CASES IN WHICH DIFFERENCE IN RESULTS OBTAINED BY BOTH METHODS WAS SIGNIFICANT*

Graph Data	Computed Data	Difference	Standard Deviation
27	37	10	3.5
25	40	15	4.5
32	25	7	3.0
24	39	15	5.5
22	37	15	4.5
28	20	8	3.0
18	29	11	5.0
35	21	14	3.5

* All figures shown are in days.

In the other 22 per cent of the cases we found a large difference between the two methods in calculated half time of disappearance: the standard deviation was larger than 3 days and the difference between plotted half time and computed half time was always larger than two standard deviations.

We can say that the method of analysis presented, using a programmable calculator has proved useful in determining half time of disappearance and standard deviations for this type of work.

It is suggested that the method of "least

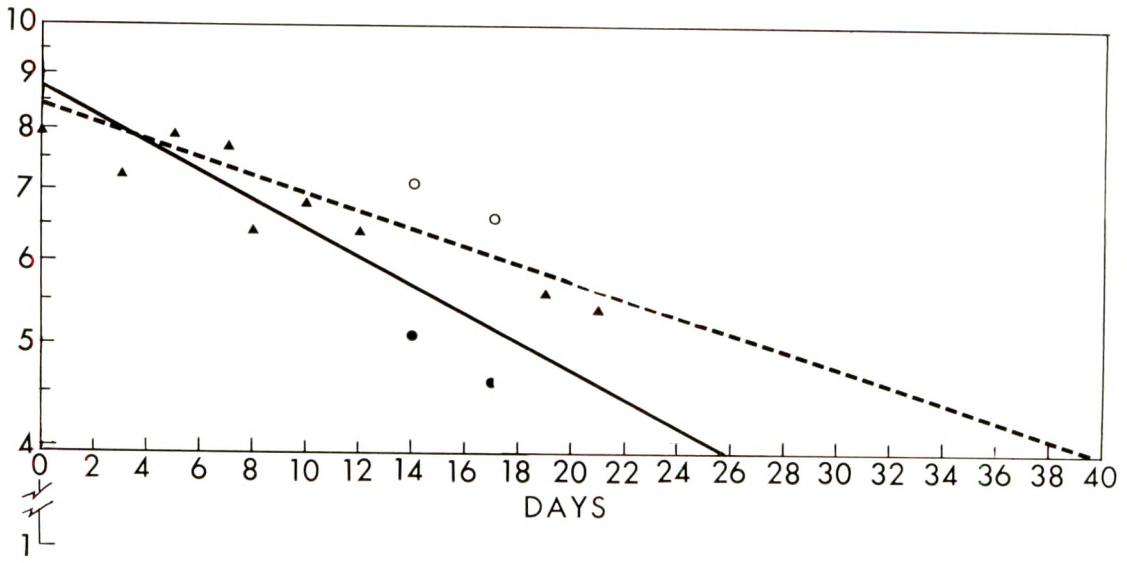


FIG. 5. Plotting errors spotted by computation.

squares" using a relatively inexpensive programmable calculator be used in the performance of routine tests of this type in the Nuclear Medicine Laboratory.

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Vol. 106, No. 4

THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

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Fifty-second Annual Meeting: Hotel Coronado, San Diego, Calif., March 1–6, 1970.

EDITORIAL

INSTRUCTION COURSES OF THE SEVENTIETH ANNUAL MEETING OF THE AMERICAN ROENTGEN RAY SOCIETY

PRESIDENT-ELECT James C. Cook, Chairman of the Program Committee, requested Dr. Harold O. Peterson, Director, and Dr. Donn G. Mosser, Associate Director of the Section on Instruction, to again arrange Instruction Courses for the Seventieth Annual Meeting of the American Roentgen Ray Society, which will be held at the Washington-Hilton Hotel, Washington, D. C., September 30 to October 3, 1969.

These courses were inaugurated exactly 30 years ago by Dr. Edward L. Jenkinson, President-Elect of the Fortieth Annual Meeting of the Society in Chicago, Illinois. Since then, year after year, they contributed outstandingly to the over-all success of the Annual Meeting, by bringing to members and nonmembers alike, in a rather informal way, the latest information on subjects of educational, experimental and practical clinical nature.

During these 3 decades there were 3 brilliant Directors serving the Society: Dr. B. R. Kirklin, 1939–1948; Dr. H. M. Weber, 1948–1957; and Dr. Harold O. Peterson, 1957–1969 (with the exception of 1964, the year of his tenure of office as President-Elect, when Dr. Donn G. Mosser substituted).

The Society is extremely fortunate to have this year Dr. Harold O. Peterson, the Director with the longest experience, again take charge of this important part of the Annual Meeting. He, assisted by Dr. Donn G. Mosser, assembled a distinguished Faculty of Instructors, representing the most renown authorities in their fields.

Judging from a perusal of the abstracts on the following pages, the Instruction Courses this year excell in all respects.

The Section on Instruction will present a total of 47 courses: 13 each on Tuesday, Wednesday and Thursday; and 8 on Friday. Some of the courses will be in 2 sessions. The following is the distribution according to various categories: (1) Diagnostic Roentgenology, 18 single period, and 11 double period; (2) Therapeutic Radiology, 4 single period; (3) Nuclear Medicine and Allied Sciences, 3 single period courses.

The Meeting Rooms in which the Instruction Courses will be held are large, comfortable, and all are air-conditioned. The respective assignments will be found at the Special Registration Desk.

A list of the distinguished Faculty and a brief abstract of each course, as well as the schedule of the courses and the registration form with the appropriate instructions, are published in the following pages of this issue of the JOURNAL.

Director Harold O. Peterson recommends a registration as early as possible.

Vol. 106, No. 4

AMERICAN ROENTGEN RAY SOCIETY

SECTION ON INSTRUCTION

Harold O. Peterson, M.D., *Director*
Donn G. Mosser, M.D., *Associate Director*

Titles and Abstracts of Courses Offered
Seventieth Annual Meeting
Washington-Hilton Hotel, Washington, D. C.
September 30–October 3, 1969

The Instruction Courses for the Seventieth Annual Meeting of the American Roentgen Ray Society will be held on Tuesday, Wednesday and Thursday afternoons, September 30, October 1 and 2 at 3:00 P.M., and Friday afternoon, October 3 at 1:30 P.M. Each course will be of 90 minutes' duration and no other official activity will be scheduled for this time.

A special registration desk for these courses will be located near the general registration area. Complete information concerning the courses as well as tickets for the courses will be available on Monday, September 29 from 8:30 A.M. to 4:00 P.M. and daily the rest of the week. Thirteen daily courses will be given on Tuesday, Wednesday and Thursday, and eight on Friday. Please note that some of the courses will be given in two sessions. A brief abstract for each course will be found on the following pages as well as a complete list of the faculty and the registration form.

Admission to all courses will be by ticket. To avoid the confusion usually present on the first day, tickets will be mailed to everyone whose registration forms (Pink Sheets) reach the office of the Director before September 20, 1969. Please watch for your tickets which will be sent in an envelope marked: Section on Instruction—American Roentgen Ray Society—Tickets Enclosed.

All orders will be filled according to the postmark on the envelopes and the First Mailing Will Be About September 5, 1969.

HOW TO REGISTER AND OBTAIN TICKETS

Review the abstracts on the following pages; make three choices for each day; fill out the pink order sheet with the course number and name of instructor for each choice. For *each course* selected a $3.00 registration fee is required from *nonmembers*. Four tickets, one for each day, may be purchased for $10.00, but single tickets are $3.00 each.

Members of the American Roentgen Ray Society, graduate students or residents in Radiology, and nonmembers who are contributing to the program either by way of an instruction course, a paper or a scientific exhibit, are not required to pay for these courses but must fill out a Pink Order Sheet indicating their choices.

If your advance registration reaches the office of the Director after September 20, 1969, you may obtain your tickets at the Registration Desk of the Section on Instruction at the hotel on Monday afternoon, September 29, 1969, and thereafter.

Please mail your order sheets to Dr. Harold O. Peterson, 1995 West County Road "B", St. Paul, Minnesota 55113.

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DESCRIPTION OF COURSES

COURSE 101
and
COURSE 201

Tuesday and Wednesday

ALEXANDER S. MACMILLAN, JR., M.D.
Boston, Massachusetts

Course 101. The Temporal Bone by Conventional Studies Exclusive of the Polytome

Course 201. Orbits, Sinuses, and Nasopharynx by Plain Film Roentgenography, Special Studies, and Laminagraphy Exclusive of the Polytome

Following a discussion of positioning, normal and some acceptable variations of the normal plus various pathologic states will be presented. As much information as possible will be given in as short a time as possible.

Following the presentation there will be an opportunity for questions.

COURSE 102
and
COURSE 202

Tuesday and Wednesday

BENJAMIN FELSON, M.D.
Cincinnati, Ohio

Course 102. Diffuse Lung Lesions

The problem of differential diagnosis of the vast array of disseminated pulmonary lesions is an almost insurmountable one unless specific patterns can be identified on the roentgenogram. It is often possible to recognize the diffuse alveolar pattern and, once identified, the list of its causes is relatively short. The recognition of diffuse interstitial disease is considerably more difficult, but even here it is sometimes possible to reliably distinguish this pattern and thereby reduce the etiologic possibilities to a reasonable number. In this course the roentgen features of the alveolar and interstitial patterns will be described and the various causes of each will be illustrated.

Course 202. Abdominal Gasmanship

COURSE 103

Tuesday

SADEK K. HILAL, M.D.
New York, New York

Cerebral Angiography: Technical Remarks

The technical aspects of cerebral angiography will be presented with particular emphasis on the choice of the proper procedure to suit the clinical situation. A discussion of the various radiographic projections will be presented. The subject of equipment for cerebral angiography will be covered.

The presentation will include the following topics:

1. Discussion of the various techniques of cerebral angiography: carotid, brachial and vertebral angiography, catheter techniques and contrast media
2. Complications and safety measures
3. The choice of the appropriate procedure and the

modification of such choice as the test proceeds
4. The radiographic projections
5. The radiographic equipment used in cerebral angiography

COURSE 104

Tuesday

NORMAN E. CHASE, M.D.
New York, New York

IRVIN I. KRICHEFF, M.D.
New York, New York

Angiography of Cerebral Vascular Occlusive Disease

This course will discuss the over-all approach to the angiographic investigation of the patient with occlusive cerebral vascular diseases. Topics will include the philosophy of total cerebral angiography and a survey of current techniques with a detailed discussion of our own angiographic technique.

Extracranial and intracranial stenotic lesions and collateral circulation will be demonstrated.

The incidence of lesions in specific locations and complications of angiography will also be reviewed.

COURSE 105

Tuesday

GUY D. POTTER, M.D.
New York, New York

Roentgenology of the Orbits

1. The normal roentgenographic anatomy of the orbit
   a. Conventional roentgen anatomy
   b. Tomographic anatomy
2. Pathologic roentgenographic anatomy
   a. Trauma to the orbits
   b. Orbital tumors
   c. Exophthalmos
   d. Vision loss
3. Normal and abnormal optic canals
   a. Conventional roentgenography
   b. Tomography
4. Clinical-roentgenologic correlation
   a. What pathologic ophthalmologic conditions are likely to demonstrate roentgenographic changes?
   b. How can the radiologist be helpful in aiding the ophthalmologist in determining diagnosis, prognosis, and surgical approach?

COURSE 106

Tuesday

CHAS. E. SHOPFNER, M.D.
Kansas City, Missouri

Current Status of Pediatric Uroradiology—Results of a Five Year Evaluation

Pediatric uroradiology has passed through several eras in the last 5 years.

In the beginning it was an iconoclastic period during which many concepts were exploded as myths. An intermediate period of agonizing re-evaluation and re-appraisal occurred which established a basis for the third era. It has been an exciting and revealing one in which all aspects of pediatric uroradiology, such as method of examination, normal anatomy, contrast agents, and new pathologic concepts have been explored by sound clinical investigation and study, and for the first time free of the bondage of the pathologic myths of the past.

Urinary tract infection remains the predominant problem of the fetus, infant and child. Newer concepts of the etiology, pathogenesis, and pathology of urinary tract infection maintain roentgenology as the most important method in its investigation.

COURSE 107

Tuesday

ANTHONY F. LALLI, M.D.
Ann Arbor, Michigan

The Tailored Urogram

The basic principles involved in executing and interpreting excretory urograms will be discussed with emphasis placed upon the tailoring of the examination to the particular problems of the individual patient. The indications for the assorted types of urograms will be detailed and the methods involved presented.

Medullary sponge kidney disease, pyelonephritis, the infrequent voiding syndrome, and renal cysts and neoplasms will be some of the subjects to be covered.

The techniques of laminagraphy, percutaneous renal mass puncture and antegrade pyelography will also be included.

The problems of dosage in the presence of renal failure, the reactions to contrast media, and other facets of the examinations will be discussed to provide a guide to the best utilization of these examinations.

COURSE 108

Tuesday

EDWARD B. SINGLETON, M.D.
Houston, Texas

Pediatric Pulmonary Abnormalities

I. Pulmonary expansion at birth
II. The normal neonatal chest
III. Pulmonary causes of neonatal respiratory distress

1. Transient tachypnea of the newborn (transitional distress syndrome)
2. Hyaline membrane disease
3. Intrauterine aspiration syndrome
4. Pulmonary hemorrhage
5. Aspiration pneumonia
6. Intrauterine infectious pneumonia
7. Congenital lobar emphysema
8. Cystic adenomatoid malformation
9. Pulmonary dysmaturity
10. Congenital lymphangiectasia
11. Congenital subpleural blebs and interstitial emphysema

11. Congenital subpleural blebs and interstitial emphysema

12. Pneumothorax
13. Alveolar hypoplasia
14. Double diaphragm
15. Tracheal stenosis and laryngeal stridor

IV. Pulmonary abnormalities in infants diagnosed by lung biopsy
1. Pneumocystis pneumonia
2. Cytomegalic inclusion disease
3. Nonspecific interstitial pneumonitis
4. Pulmonary alveolar proteinosis
5. Desquamative interstitial pneumonia
6. Lymphocytic interstitial pneumonia
7. Pulmonary vasculopathy
8. Pulmonary telangiectasia
9. Pulmonary lymphangiectasia
10. Idiopathic hemosiderosis
11. Pulmonary eosinophilic granuloma
12. Alveolar microlithiasis

V. Unusual pneumonias of infants and children
1. Ectodermal dysplasia
2. Aldrich's syndrome
3. Giant cell pneumonia
4. Nocardiosis
5. Mucormycosis
6. Coccidioidomycosis

COURSE 109

Tuesday

BERNARD S. WOLF, M.D.
New York, New York

Roentgen Features of the Normal and Herniated Esophagogastric Region: Clinical Correlations

Difficulties in defining exact criteria for the presence of a small sliding hiatus hernia have obscured the important practical problem, that is, to determine whether there are objective roentgen findings in a specific case which are sufficient to explain the patient's symptoms.

Prophylactic surgical therapy for a small asymptomatic sliding hernia is not indicated. An effort will be made, therefore, to describe roentgen features to be expected in the patient who presents with the chief complaint of: (1) heartburn; (2) dysphagia; (3) chest pain; (4) gross bleeding; and (5) anemia.

The roentgen features of an "asymptomatic" sliding hernia, either small or large, will also be indicated.

Since the selection of therapy must depend on an analysis of the cause of symptoms, the roentgen evaluation, confirmed when necessary by manometric studies, is of considerable importance. Such an analysis is also necessary in deciding the goals of operative intervention and in judging objectively the effectiveness of such therapy.

COURSE 110

Tuesday

JOHN A. CAMPBELL, M.D.
Indianapolis, Indiana

The Diaphragm

The diaphragm is visualized in over 50 per cent of the various examinations viewed by roentgenologists, and its configuration is often of diagnostic significance. As the Greek term "Diaphragma," meaning partition, implies, its importance in separating the thoracic and abdominal cavities is rarely appreciated until some breakdown of this function ensues.

Knowledge of the wide variety of abnormalities and variations involving the diaphragm is of practical usefulness in distinguishing primary disorders from secondary changes associated with thoracic or abdominal disease. Proper identification of the type and origin of lesions affecting the diaphragm is an important consideration in determining the advocacy as well as the selection of corrective surgery.

The following roentgen aspects of the diaphragm will be presented:

1. Anatomy and normal variations
2. Anomalies and malformations
3. Position and contour
4. Eventration and paresis
5. Subpulmonary and subphrenic lesions
6. Hernias and traumatic changes
7. Tumors and cysts

COURSE 111

Tuesday

ISADORE MESCHAN, M.D.
Winston-Salem, North Carolina

RICHARD JANEWAY, M.D.
Winston-Salem, North Carolina

C. DOUGLAS MAYNARD, M.D.
Winston-Salem, North Carolina

JOSEPH E. WHITLEY, M.D.
Winston-Salem, North Carolina

Radiology (Including Nuclear Medicine) in Neurovascular Diagnoses

This presentation will include a summary of the various techniques used in diagnostic radiology and nuclear medicine for the evaluation of patients with neurovascular disease.

Consideration will be given to the relative merits of the procedures involved.

COURSE 121

Tuesday

JUAN A. DEL REGATO, M.D.
Colorado Springs, Colorado

Radiotherapy for Cancer of the Prostate Gland

Radical radiation therapy is a curative approach to the treatment of cancer of the prostate beyond the eligibility of the given case for radical surgery.

Radiation therapy is accompanied with little discomfort and is followed by no important complications.

COURSE 122

Tuesday

PETER JAMES FITZPATRICK M.D.
Toronto, Ontario, Canada

The Place of Radiotherapy in the Management of Lymphomas

The differences in the clinical manifestations and in the clinical course will be discussed with reference to Hodgkin's disease, lymphosarcoma and reticulum cell sarcoma. A knowledge of these variations is helpful in the management of the individual patient since it allows one to anticipate the expected course and prescribe accordingly.

The curative approach will be stressed for the groups of patients offering a good prognosis and the plan of management will be presented for each stage of the disease in each morphologic group.

The complications in the clinical management of these patients will be discussed with special reference to iatrogenic problems associated with more aggressive therapy in attempts at cure.

COURSE 203
and
COURSE 303

Wednesday and Thursday

ELIAS G. THEROS, M.D.
Washington, D. C.

Course 203. The Evaluation of Diffuse Parenchymal Lesions of the Lungs

A Radiologic-Pathologic Correlative Study

The broad gamut of diseases that cause diffuse changes in the pulmonary parenchyma usually result in discouragingly similar patterns that defy specific diagnostic labeling without the help of pertinent clinical and laboratory data. Nevertheless, these patterns can be studied in considerable detail and grouped into meaningful categories that allow the radiologist to indicate whether a process is basically interstitial, alveolar, or a mixture of these, and infer whether the process is transitory or of long standing. Thus, it is worthwhile to review the roentgen signs by which such evaluations can be made and particularly to seek more understanding and documented explanations for them by correlating them with the gross and low power histologic findings of the pathologist. Only through such correlated anatomic study will the radiologist gain proper understanding of the disturbed morphology underlying the roentgen signs and thus sharpen his diagnostic powers in a challenging and difficult area.

Course 303. Granulomatous Diseases of the Lung

A Radiologic-Pathologic Correlative Study

Man is beset by a multitude of agents that may trigger granulomatous reactions in the pulmonary tissues. The variation in his ability to resist and contain them gives rise to a number of localized and diffuse morphologic changes which are reflected in a wide gamut of roentgenographic patterns. A spectrum of such patterns will be presented and correlated with the gross and histologic findings. Although such roentgen patterns are frequently not diagnostic enough for specific labeling, they are often reliably characteristic. Such characteristics will be stressed and explanations for them sought in the pathogenesis of these diseases or in the disturbed morphology noted by the pathologist.

In any such review, the fungi are of great importance, not only because they yield a veritable panorama of roentgen patterns for consideration, but also because they are an increasing clinical problem resulting from the recent widespread use of antibiotics, steroids, and cytotoxic agents. The fungi, therefore, will be given special attention but a survey will be made of the important categories of agents that cause granulomatous response in the lungs: the pneumoconioses, histiocytosis, sarcoidosis, acid-fast disease, and the collagen diseases.

COURSE 204
and
COURSE 304

Wednesday and Thursday

RICHARD H. MARSHAK, M.D.
New York, New York

Course 204. The Small Bowel

The following topics will be discussed:

1. Technique
2. The malabsorption syndrome. This is a continuous topic discussed every year and brought up to date. New lesions are constantly being described such as hypogammaglobulinemia, lymphoid hyperplasia, endocrine abnormalities, etc.
3. Carcinoids
4. Lymphosarcoma
5. Metastatic lesions

Course 304. The Colon

1. Technique
2. Diverticulitis and its relationship to granulomatous colitis
3. Tumors of the colon, excluding carcinoma
   The question of polyps is far from settled. Additional data will be presented
5. Newer lesions will be discussed

COURSE 205
and
COURSE 305

Wednesday and Thursday

WILLIAM MARTEL, M.D.
Ann Arbor, Michigan

Joint Diseases

Course 205. Part I

Emphasis will be placed on practical points in the diagnosis of common diseases and new observations will be stressed. The first session will deal with rheumatoid arthritis, villonodular synovitis, osteoarthritis, gout, pseudogout, neuropathic joints and osteonecrosis.

The discussions (both in this Course and in Course 305) will be given in the context of differential diagnosis and, consequently, a number of conditions not mentioned here will be shown to illustrate various points.

Course 305. Part II

This will be given in the same fashion as Course 205 and the following diseases, among others, will be discussed: ankylosing spondylitis, rheumatoid arthritis (spine), juvenile rheumatoid arthritis, psoriasis, Reiter's disease, scleroderma, occupational acro-osteolysis, infectious arthritis and miscellaneous conditions.

COURSE 206
and
COURSE 306

Wednesday and Thursday

WILLIAM E. GANNON, M.D.
Brooklyn, New York

Carotid Angiography

Course 206. Part I

Normal anatomy
Occlusions
- (a) Internal carotid artery
- (b) Intracranial arteries

Aneurysms
Arteriovenous malformations
Head trauma
- (a) Subdural hematoma
- (b) Epidural hematoma
- (c) Internal carotid artery-cavernous sinus fistula
- (d) Intracerebral hematoma and cerebral contusion

Course 306. Part II

General signs of space-saving lesions
Tumors
- (a) Meningiomas
- (b) Gliomas
- (c) Metastatic lesions

Tentorial herniation

COURSE 207

Wednesday

D. GORDON POTTS, M.D.
New York, New York

Pneumoencephalography and Ventriculography Techniques and Anatomy

The following aspects will be discussed:

1. Mechanism of filling of ventricles and methods of demonstrating cisterns during pneumoencephalography
2. Manipulation of air during ventriculography
3. Projections used during these studies
4. Modern methods of examination of a patient with a suspected 8th nerve tumor
5. Anatomy of the ventricles demonstrated by brain specimens
6. Anatomy of the subarachnoid cisterns

COURSE 208

Wednesday

HERMAN GROSSMAN, M.D.
New York, New York

Radiography of Childhood Tumors

Special procedures, as well as gastrointestinal studies and intravenous pyelography, will be discussed. Indications and limitations of angiography, lymph-

angiography and radioactive isotopes in children will be stressed.

Gastrointestinal lesions will include the stomach, small bowel, gallbladder, liver and pancreas.

Retroperitoneal tumors are relatively common and many of these are benign. Wilms' tumor and neuroblastoma, usually malignant tumors, constitute the most significant varieties numerically in this site. A variety of retroperitoneal mass lesions in children will be shown and a radiographic approach will be suggested.

COURSE 209

Wednesday

DAVID H. BAKER, M.D.
New York, New York

WALTER E. BERDON, M.D.
New York, New York

Roentgen Manifestations of Acquired Bone Disease in Children

Acquired bone lesions in children are, in many instances, the result of the same disease state seen in adults. The child, however, is growing and because of this growth the roentgen manifestations tend to be very different from those seen in the adult.

We will illustrate this difference by showing and discussing longitudinal studies on:

1. The abused child ("battered child")
2. Rheumatoid arthritis
3. Bone and joint infection
4. Long term survivors of irradiation
5. The hemoglobinopathies
   a. Sickle cell disease
   b. Cooley's anemia
6. Intoxication with various substances
7. Deficiency states
8. Storage diseases
9. Neurologic disorders

COURSE 210

Wednesday

DAVID M. WITTEN, M.D.
Rochester, Minnesota

Mammography

This course covers in detail the technique of mammography, the principles of radiographic diagnosis and differential diagnosis, and the place of mammography in the evaluation of diseases of the breast.

COURSE 211

Wednesday

EUGENE GEDGAUDAS, M.D.
St. Paul, Minnesota

A Fundamental Approach to Plain Film Roentgenographic Evaluation of the Heart

This course will emphasize the value and limitations of plain film roentgenographic examination of the heart and great vessels.

The course will offer a method of analysis enabling the radiologist to make at least a working diagnosis, and often a definitive diagnosis, prior to cardiac catheterization or angiocardiography.

The appearance of the normal heart will be evaluated in various age groups with emphasis placed on the total examination of the heart (4 views and indications for fluoroscopy).

Changes in configuration and size beyond this normal range will be considered within the context of a roentgenologic-physiologic classification of congenital and acquired heart disease.

COURSE 221

Wednesday

JOHN G. McAFEE, M.D.
Syracuse, New York

Current Status of Radioisotopic Imaging

This course will cover the current status of scanning techniques.

The current techniques of rectilinear scanning will be discussed.

The use of scintillation cameras and utilization of short-lived radio pharmaceuticals will be emphasized.

COURSE 222

Wednesday

ELEANOR D. MONTAGUE, M.D.
Houston, Texas

Radiation Therapy in the Management of Breast Cancer

Irradiation plays an increasing role in the primary management of breast cancer as the local disease is more advanced; however, even in the earlier stages, a combination of irradiation and surgery is effective in decreasing local recurrences.

Policies of treatment at the University of Texas M. D. Anderson Hospital and Tumor Institute at Houston will be reviewed for all stages of disease:

(1) Radical mastectomy followed by irradiation of the peripheral lymph node areas, with or without chest wall irradiation
(2) Preoperative irradiation followed by radical mastectomy
(3) Radiation therapy alone for clinically inoperable local disease

The indications, techniques, and results of treatment will be discussed.

COURSE 301 and COURSE 401

Thursday and Friday

J. S. DUNBAR, M.D.
Montreal, P. Q., Canada

Course 301. Pediatric Radiology of the Gastrointestinal Tract

This course will cover a number of entities of the gastrointestinal tract of the infant and child which can be investigated by contrast media.

Emphasis will be placed on the relation of the planned investigation to the presenting complaints, and will include investigation of swallowing disorders, vomiting, abdominal pain, gastrointestinal bleeding, steatorrhea, constipation, and intestinal obstruction.

For each of these entities, the method of investigation most suitable to the presenting complaint will be outlined, followed by demonstration of conditions most likely to be encountered.

Course 401. The Chest in Pediatric Radiology

This course will emphasize assessment of chest disease by plain films, fluoroscopy, and occasionally use of esophageal contrast medium.

The entities discussed will include: infiltrative diseases of the lung, chronic inflammation including aspiration pneumonia, lower respiratory tract obstruction, circulatory disturbances, cystic disease, and congenital malformations.

There will also be discussion of pleural disease—its recognition and assessment.

COURSE 302 and COURSE 402

Thursday and Friday

HAROLD O. PETERSON, M.D.
Minneapolis, Minnesota

STEPHEN KIEFFER, M.D.
Minneapolis, Minnesota

Course 302. Myelography

These two periods will cover the technique of pantopaque myelography including posterior fossa examinations. Pantopaque myelography should be essentially painless and all of the contrast medium should be removed. The details and fine points on how to do this will be stressed. In addition, Course 302 will include discussion of the normal myelogram, the anatomic variants, and then concentrate on the diagnosis of the herniated intervertebral disk and the many confusing deformities which are often asymptomatic.

Course 402.

Cervical myelography and posterior fossa studies will be covered in this period, including cervical herniated disks, cervical spondylosis and some posterior fossa lesions.

In addition, cord tumors as well as a number of other abnormalities will be discussed, such as arachnoiditis, diastematomyelia scoliosis, trauma, large dural sac, arachnoid cysts, spinal dysraphism, Arnold-Chiari malformation and vascular abnormalities.

COURSE 307 and COURSE 407

Thursday and Friday

GALDINO E. VALVASSORI, M.D.
Chicago, Illinois

Course 307. The Normal and Abnormal Internal Auditory Meatus and Facial Nerve Canal

It is the purpose of this presentation:

1. To describe the various radiographic techniques available for the study of the facial nerve canal, internal auditory meatus and cerebellopontine angle cistern
2. To review the normal radiographic anatomy of the facial nerve canal and internal auditory meatus
3. To illustrate the changes occurring in the above structures in various pathologic conditions with special emphasis on acoustic neuromas

Course 407. The Abnormal Temporal Bone: Congenital Malformations and Cholesteatomas

Two pathologic conditions in which radiography has been of great value in the diagnosis and benefit to surgical otolaryngology will be discussed:

1. Congenital malformations subdivided into anomalies of the external and middle ear producing a conductive type of hearing loss, and anomalies of the inner ear producing sensorineural hearing loss and vestibular loss

2. Cholesteatomas, special emphasis being placed on the correlation between the radiographic findings and surgical pathology

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COURSE 308
and
COURSE 408

Thursday and Friday

HAROLD G. JACOBSON, M.D.
New York, New York

STANLEY S. SIEGELMAN, M.D.
New York, New York

Skeletal Radiology: A Potpourri of Interesting and Infrequently Encountered Lesions

In these two sessions a variety of skeletal abnormalities will be presented. Emphasis will be placed on the more esoteric lesions or unusual manifestations of commonplace conditions. For the most part solitary lesions, both benign and malignant, will be featured.

In the presentation of the illustrative material the radiologic criteria and differential diagnoses will be stressed in such a manner that the evaluation of this panorama of interesting lesions will serve as a focus for the understanding of the principles of radiologic diagnosis of skeletal disease.

The first course will deal exclusively with benign conditions and the second course with malignant lesions.

COURSE 309
and
COURSE 405

Thursday and Friday

SIDNEY W. NELSON, M.D.
Columbus, Ohio

Course 309. Bronchography

The radiologist who can properly perform and interpret bronchograms can make outstanding contributions to the diagnosis and understanding of many broncho-pulmonary diseases. Following a brief discussion of bronchial anatomy, anesthetic agents, contrast media, and techniques, the following different types of broncho-pulmonary pathology will be demonstrated:

1. Chronic bronchitis
2. Segmental bronchiectasis
3. Bronchogenic carcinoma
4. Bronchial adenoma
5. Cavitary and cystic lesions
6. Pulmonary granulomas
7. Bronchial relocation following atelectasis or surgical removal

After the demonstration of the bronchographic findings of the above listed broncho-pulmonary diseases, the value of bronchography in the differential diagnosis of a group of test cases will be illustrated. This will enable the participants to evaluate what they have learned during the course, and hopefully encourage participating radiologists to perform this extremely useful roentgenographic procedure.

The instructional manual used in the course will *only* be given to those participants who register for and attend the course.

Course 405. The Discovery of Gastric Ulcers and the Differential Diagnosis Between Benignancy and Malignancy

The discovery of gastric ulcers and the differential diagnosis between benignancy and malignancy are common problems which often present difficulties. After a brief description of the author's technique of examining the stomach and duodenum, the following differential diagnostic signs will be discussed and demonstrated:

1. *Signs of benignancy*
   - A. The penetrating sign
   - B. Mucosal folds radiating to the edge of the crater
   - C. Hampton's line
   - D. Ulcer collar
   - E. Ulcer mound
   - F. Blood clot in floor of crater
   - G. Concavo-convex ("quarter moon") shaped barium collection
2. *Signs of malignancy*
   - A. Carman's meniscus sign
   - B. Kirkland's meniscus complex
   - C. The abrupt transition sign
   - D. Nodularity of the tissue surrounding the crater
3. *Nonspecific criteria*
   - A. Intraluminal location of the crater
   - B. The "ring shadow"
   - C. Size of the crater
   - D. Location of the crater
   - E. Shape of the crater
   - F. Change of size of the crater during treatment

Those craters which do not clearly show reliable signs of benignancy or malignancy should be termed "indeterminate." The proper spot roentgenograms of gastric ulcers, utilizing maneuvers designed to bring out the above mentioned diagnostic signs of benignancy and malignancy with techniques which *profile* the crater, will result in the highest rate of diagnostic accuracy.

COURSE 310

Thursday

GEORGE JACOBSON, M.D.
Los Angeles, California

HARVEY MEYERS, M.D.
Los Angeles, California

The Acute Abdomen: Intestinal Obstruction and Other Selected Conditions

Intestinal Obstruction: A logical approach to the roentgenographic diagnosis of small and large bowel obstruction will be presented relating the roentgen features to alter physiology. The recognition of vascular impairment will be stressed.

Perforated Peptic Ulcer: The use of a water-soluble contrast medium to examine the upper gastrointestinal tract of patients suspected of having perforated peptic ulcer and the rationale for the procedure will be discussed.

Non-penetrating Injuries of the Abdomen: The discussion will pertain to the roentgen manifestations in blunt trauma to the gastrointestinal tract, liver and spleen.

COURSE 311

Thursday

RICHARD A. ELMER, M.D.
Atlanta, Georgia

70 mm. Spot Filming

The major purpose of this presentation will be to discuss factors peculiar to photofluorography; *i.e.*, factors having a bearing on desirable image quality. The following subjects will be considered:

1. Intensifier tubes
2. Camera lenses
3. X-ray tubes (focal spot sizes, ma, and kv.)
4. Film types and methods of processing

Factors affecting speed in the system and factors related to film size, anatomic coverage, and film cost will also be discussed.

COURSE 321

Thursday

MARVIN M. D. WILLIAMS, Ph.D.
Rochester, Minnesota

Preparing for an Examination in Radiological Physics

The answers given to various types of questions in radiological physics, although not entirely incorrect are often unsatisfactory. Frequently, the answer given is an equation, a numerical constant, or a memorized statement. The examinee frequently cannot tell (1) what conditions must be satisfied in order that the use of the equation is justified, (2) what the numerical constant represents, or (3) what the memorized statement means. This problem and some of these questions will be discussed with the aim not only of indicating a correct answer but also of showing that an acceptable answer is likely to follow naturally when the subject matter is understood. The discussion will include suggestions from other examiners in radiological physics.

COURSE 322

Thursday

GIULIO J. D'ANGIO, M.D.
New York, New York

The Management of Children with Abdominal and Pelvic Tumors

The common tumors involving the abdomen and pelvis will be discussed. Included will be the Wilms' tumor, neuroblastoma, genital tumors in girls, and vesico-prostatic tumors in boys.

Vagaries of these neoplasms will be discussed in detail, methods of management outlined, and results presented. The role of radiotherapy will be stressed, but surgical and chemotherapeutic implications will be encompassed in the presentation.

COURSE 403

Friday

LEWIS E. ETTER, M.D.
Pittsburgh, Pennsylvania

Normal and Pathologic Roentgen Anatomy of the Skull

Description of standard techniques and positions with illustrated slides for roentgen examination of the skull.

Comparison of advantages of one projection over another with respect to visibility of particular structures.

General considerations with reference to the cerebral and facial components of the cranium with analysis of individual bone components that produce the various lines and shadows seen in plain roentgenograms of the skull.

Examples of pathologic alterations of these normal structures will be shown.

The analysis will cover studies of the sphenoid, frontal, temporal, ethmoid, parietal and occipital bones in various projections.

COURSE 404

Friday

HELEN C. REDMAN, M.D.
Eloise, Michigan

STEWART R. REUTER, M.D.
San Diego, California

Visceral Angiography

Visceral angiography is a relatively recent angiographic subspecialty and is still in the process of development.

Several important applications of the method to the evaluation of visceral disease have already been established. These include use in the evaluation of vascular disease, gastrointestinal bleeding, trauma, visceral tumors, and visceral inflammatory lesions.

Introductory remarks will be made about technique and anatomy.

COURSE 406

Friday

JOSEPH R. CASTRO, M.D.
Houston, Texas

Cancer of the Uterine Cervix and Its Clinical Management

This course will cover basic techniques in the treatment of carcinoma of the uterine cervix at the M. D. Anderson Hospital and Tumor Institute.

The important aspects of external radiation therapy and radium therapy will be covered. Attention will be given to the clinical varieties of these tumors, routes of spread and special clinical situations as correlated with therapeutic approaches.

Discussion of treatment of lymphatics, including utilization of extended fields will be included. A brief analysis of therapeutic results, including survival, local control rates and complication incidence, will be given.

CONDENSED SCHEDULE OF COURSES

TUESDAY 3:00 to 4:30 P.M. September 30, 1969

101—Macmillan
The Temporal Bone

102—Felson
Diffuse Lung Lesions

103—Hilal
Cerebral Angiography

104—Chase
Kricheff
Angiography of Cerebral Vascular Occlusive Disease

105—Potter
Roentgenology of the Orbits

106—Shopfner
Current Status of Pediatric Uroradiology

107—Lalli
The Tailored Urogram

108—Singleton
Pediatric Pulmonary Abnormalities

109—Wolf
Roentgen Features of the Normal and Herniated Esophagogastric Region

110—Campbell
The Diaphragm

111—Meschan
Janeway
Maynard
Whitley
Radiology (Including Nuclear Medicine) in Neurovascular Diagnoses

121—del Regato
Radiotherapy for Cancer of the Prostate Gland

122—Fitzpatrick
The Place of Radiotherapy in the Management of Lymphomas

CONDENSED SCHEDULE OF COURSES

WEDNESDAY 3:00 to 4:30 P.M. October 1, 1969

201—Macmillan
Orbits, Sinuses and Nasopharynx by Plain Film Roentgenography, Special Studies and Laminagraphy

202—Felson
Abdominal Gasmanship

203—Theros
The Evaluation of Diffuse Parenchymal Lesions of the Lungs

204—Marshak
The Small Bowel

205—Martel
Joint Diseases—Part I

206—Gannon
Carotid Angiography—Part I

207—Potts
Pneumoencephalography and Ventriculography: Techniques and Anatomy

208—Grossman
Radiography of Childhood Tumors

209—Baker
Berdon
Roentgen Manifestations of Acquired Bone Disease in Children

210—Witten
Mammography

211—Gedgaudas
A Fundamental Approach to Plain Film Roentgenographic Evaluation of the Heart

221—McAfee
Current Status of Radioisotopic Imaging

222—Montague
Radiation Therapy in the Management of Breast Cancer

SECTION ON INSTRUCTION

ORDER SHEET

It is important to register for the Instruction Courses as early as possible since the number admitted to each course will be limited. *It is also very important that first, second and third choices be listed for each period.* All orders for tickets will be filled according to the postmark on the envelopes.

Nonmembers of the American Roentgen Ray Society will pay $3.00 for each course-period or a maximum of $10.00 for 4 courses. *Nonmembers' fees must accompany this Order Sheet and will not be returned unless cancellation is received before September 24, 1969.*

Members of the American Roentgen Ray Society, graduate students or residents in Radiology, and nonmembers who are contributing to the program, either by way of an instruction course, a paper or a scientific exhibit, are not required to pay for these courses but must fill out these Pink Order Sheets, indicating their choices.

Tickets for courses will be mailed to each registrant whose order reaches the office of the Director on or before September 20, 1969. They will be sent to the address below unless registrant directs otherwise.

Please fill out the following (type or print):

....
Last Name First Name or Initials

....
Street Address

....
City State Zip Number

Check ☐Member ☐Guest ☐Graduate Student in Radiology at: ..... ☐Scientific Exhibitor/Paper

Those whose advance registration reaches the office of the Director after September 20, 1969 may obtain their tickets at the Registration Desk of the Section on Instruction on Monday afternoon, September 29, 1969 and thereafter. At this time tickets may also be obtained for courses not sold out.

For convenience in selecting your courses consult the condensed schedule of courses.

BE SURE TO FILL OUT SECOND AND THIRD CHOICES FOR EACH PERIOD

Period	First Choice		Second Choice		Third Choice	
	Course No.	Instructor	Course No.	Instructor	Course No.	Instructor
Tuesday						
Wednesday						
Thursday						
Friday						

Send this order to:
DR. HAROLD O. PETERSON, 1995 West County Road "B", St. Paul, Minnesota 55113

CONDENSED SCHEDULE OF COURSES		
THURSDAY	3:00 to 4:30 P.M.	October 2, 1969

301—Dunbar Pediatric Radiology of the Gastrointestinal Tract	**308—Jacobson, Harold Siegelman** Skeletal Radiology
302—Peterson Kieffer Myelography	**309—Nelson** Bronchography
303—Theros Granulomatous Diseases of the Lung	**310—Jacobson, George Meyers** The Acute Abdomen: Intestinal Obstruction and Other Selected Conditions
304—Marshak The Colon	**311—Elmer** 70 mm. Spot Filming
305—Martel Joint Diseases—Part II	**321—Williams** Preparing for an Examination in Radiological Physics
306—Gannon Carotid Angiography—Part II	**322—D'Angio** The Management of Children with Abdominal and Pelvic Tumors
307—Valvassori The Normal and Abnormal Internal Auditory Meatus and Facial Nerve Canal	

CONDENSED SCHEDULE OF COURSES		
FRIDAY	**1:30 to 3:00 P.M.**	**October 3, 1969**

401—Dunbar
The Chest in Pediatric Radiology

402—Peterson
Kieffer
Myelography

403—Etter
Normal and Pathologic Roentgen Anatomy of the Skull

404—Redman
Reuter
Visceral Angiography

405—Nelson
The Discovery of Gastric Ulcers and the Differential Diagnosis Between Benignancy and Malignancy

406—Castro
Cancer of the Uterine Cervix and Its Clinical Management

407—Valvassori
The Abnormal Temporal Bone: Congenital Malformations and Cholesteatomas

408—Jacobson, Harold
Siegelman
Skeletal Radiology

NEWS ITEMS

THE AMERICAN BOARD OF RADIOLOGY

At the Annual Meeting of The American Board of Radiology held in Pittsburgh on June 1, 1969, the Bylaws of the Board were amended to allow Osteopathic Physicians holding D.O. degrees to be examined by The American Board of Radiology if they have fulfilled all of the usual training requirements.

The Trustees of the Board voted to require A.M.A. approved internships and A.M.A. approved residencies as training requirements for Osteopaths. Although rarely the Executive Committee of The American Board of Radiology can alter these requirements in an individual case, the Trustees directed the Executive Committee to give no credit for American Osteopathic Association approved internships or residencies.

After three years of training in an approved residency program, The American Board of Radiology requires a fourth year of either further training or practice. If an Osteopath has been practicing Radiology before he enters an A.M.A. approved residency program, it is possible for the Executive Committee of the Board to give him credit for this year. It is likewise possible for the Executive Committee to give credit for service in the Armed Forces if the individual Osteopathic Physician was assigned full time to Radiology. This credit applies only to the fourth year of further training or practice.

The licensure requirement is worded as follows: "Osteopathic Physicians must have a license to practice medicine that is identical with and equivalent to the full and unrestricted licenses granted graduates of approved schools of medicine in the United States."

There are no other requirements specifically related to Osteopathic Physicians. Their training will be identical to those graduates of approved schools of medicine and the examination and practice requirements will be the same.

For further information please write to Dr. C. Allen Good, Secretary, The American Board of Radiology, Kahler Center Building, Rochester, Minnesota 55901.

ASSOCIATION OF UNIVERSITY RADIOLOGISTS ELECTS NEW OFFICERS

The Seventeenth Annual Meeting of the Association of University Radiologists was held in San Francisco, California, May 8–10, 1969, at the San Francisco Medical Center of the University of California.

The new officers of the Association for 1969–1970 are: *President*, Harry Z. Mellins, M.D., Harvard Medical School, Peter Bent Brigham Hospital, Boston, Mass. 02115; *President-Elect*, Alexander Gottschalk, M.D., University of Chicago Hospitals, Chicago, Ill. 60637; and *Secretary-Treasurer*, James J. Scatliff, M.D., University of North Carolina Medical School, Chapel Hill, N. C. 27514.

The next Annual Meeting will be held at the University of Kentucky Medical Center, Lexington, Kentucky, April 29–May 1, 1970.

ASSOCIATION OF UNIVERSITY RADIOLOGISTS

An Annual Memorial Medal Award in honor of deceased members of the Association of University Radiologists is awarded to the Resident in Radiology writing the best original paper on some aspect of radiology during the period of competition. The paper must be the work of only one author, the Resident. Manuscripts to be considered for the 1970 competition must be received by March 1, 1970.

Inquiries should be addressed and papers submitted to the Secretary-Treasurer, Dr. James J. Scatliff, University of North Carolina Medical School, Chapel Hill, North Carolina 27514.

The winner of the competition will be invited to present his work at the Annual Meeting of the Association, and will receive a monetary award in addition to the medal.

THE INTERNATIONAL COMMISSION ON RADIATION UNITS AND MEASUREMENTS (ICRU)

The International Commission on Radiation Units and Measurements (ICRU) announces that Dr. Lewis V. Spencer is the first recipient of the L. H. Gray Medal.

The medal is awarded for outstanding contributions in scientific fields of interest to the ICRU and honors the late Louis Harold Gray, former member and Vice Chairman of the Commission. Dr. Spencer, a physicist at the U. S. National Bureau of Standards and Professor of Physics at Ottawa University (Kansas), will receive the award at the XIIth International Congress of Radiology to be held in Tokyo, Japan, October 6–11, 1969.

The recipient of the medal is invited to give a scientific lecture to the ICRU and its guests. In Dr. Spencer's case, this lecture will be given during the International Congress of Radiology in Tokyo, and it will later be published in the open literature.

ALBERT EINSTEIN COLLEGE OF MEDICINE OF YESHIVA UNIVERSITY

Third Neuroradiology Postgraduate Course

The Department of Radiology of the Albert Einstein College of Medicine, Bronx, New York, will sponsor its third postgraduate course in neuroradiology May 11 to May 15, 1970.

For further information, please contact Dr. Mannie M. Schechter, Program Director, Neuroradiology Postgraduate Course, Albert Einstein College of Medicine, Bronx, N. Y. 10461.

RADIATION RESEARCH SOCIETY (RRS)

The Radiation Research Society (RRS) is most pleased to announce the 1969 recipient of the Radiation Research Society *Research Award.*

Dr. Gerald E. Adams, Research Unit in Radiobiology, Mount Vernon Hospital, Northwood, Middlesex, England, is the first recipient of this Award which is to honor an individual for outstanding contributions in radiation research. The Award was made on May 20, 1969, in conjunction with the Society's Annual Meeting in Cincinnati, Ohio.

Dr. Adams is being cited for "continued imaginative, productive and enthusiastically youthful research in pulse radiolysis as applied to both chemistry and biology."

The RRS *Research Award,* initiated in 1969, is limited to those individuals who have not reached their fortieth birthday on January 1 of the year of the Award, and is open to anyone irrespective of membership in the Radiation Research Society. The Award consists of a citation and a $1,000 bursary.

The Radiation Research Society is an international organization whose objective is to facilitate cooperative research between the disciplines of Physics, Chemistry, Biology, and Medicine in the study of the properties and effects of radiation.

The Executive Secretary of RRS is Richard J. Burk, Jr., The American University, Washington, D. C. 20016.

THE AMERICAN SOCIETY OF NEURORADIOLOGY

At the Seventh Annual Meeting of The American Society of Neuroradiology, held jointly with The American Association of Neurological Surgeons, on April 16–18, 1969 at the Sheraton-Cleveland Hotel, Cleveland, Ohio, the following officers were elected: *President,* Giovanni DiChiro, M.D.; *President-Elect,* D. Gordon Potts, M.D.; *Vice-President,* Norman Chase, M.D.; *Secretary,* Eugene V. Leslie, M.D.; and *Treasurer,* T. Hans Newton, M.D.

The next meeting will be held at the Washington-Hilton Hotel, Washington, D. C. on February 12–13, 1970.

BOOK REVIEW

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

PARAMEDICAL DICTIONARY: A PRACTICAL DICTIONARY FOR THE SEMIMEDICAL AND ANCILLARY MEDICAL PROFESSIONS. By J. E. Schmidt, M.D. Author of: Reversicon, A Medical Word Finder; Medical Discoveries, Who & When; Narcotics, Lingo and Lore; Dictionary of Medical Slang; Baby Name Finder; A Thousand Elegant Phrases; Libido; The Medical Lexicographer; Police Medical Dictionary; Practical Nurses' Medical Dictionary; Attorneys' Dictionary of Medicine and Word Finder; and others. Cloth. Pp. 424. Price, $8.75. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62703, 1969.

Paramedical Dictionary is a cyclopedic medical reference book designed for x-ray technicians, dental assistants, physical therapists, public health officers, laboratory technologists, social workers, medical secretaries, medical librarians, personnel directors, speech therapists, dietitians, optometrists, athletic directors and coaches, court stenographers, insurance claim adjusters, and other semi-medical professions.

The book contains nearly ten thousand entries in clear, nontechnical terms, which were assiduously assembled by J. E. Schimdt, M.D., famous author of many similar publications.

A valuable feature of the book is its key to accurate pronunciation, by a simple method of respelling, indicating each syllable as well as the primary and secondary accents.

The format is elegant and careful attention has been given by the Publisher to all details of manufacturing and design. The printing is of the highest quality and makes for easy reading.

There are also 2 Appendices at the end of the book. Appendix I contains a list of the Communicable Diseases, encompassing the causative agent, incubation period, communicability period, and symptoms; and there are other data of medical usefulness, such as weights, measures, equivalents and dosage tables. In Appendix II the most common medical abbreviations and symbols are compiled alphabetically and their meaning is lucidly defined.

Paramedical Dictionary is an indispensable lexicon for the Semi-Medical and Ancillary Medical Professions and as such is enthusiastically recommended.

T. LEUCUTIA, M.D.

BOOKS RECEIVED

ATLANTE DI MAMMOGRAFIA. By M. Lenzi, F. Amici, V. Marchisio, R. Romagnoli, and U. Salvolini, Istituto di Radiologia, dell'Università di Modena. Cloth. Pp. 150, with many illustrations. Editore Artioli, Modena-Milano, Italy, 1969.

CEREBRAL CIRCULATION. Progress in Brain Research. Volume 30. Edited by W. Luyendijk, Professor of Neurosurgery, Division of Neurosurgery, Academic Hospital, Leyden, The Netherlands. Cloth. Pp. 512, with some illustrations. Price, $34.00. American Elsevier Publishing Company, Inc., 52 Vanderbilt Avenue, New York, N. Y. 10017, 1969.

PROGNOSTIC FACTORS IN BREAST CANCER. Proceedings of first Tenovus Symposium, Cardiff, 12–14 April, 1967. Edited by A. P. M. Forrest, Professor of Surgery, Welsh National School of Medicine; and P. B. Kunkler, Director of Radiotherapy, United Cardiff Hospitals and South Wales Radiotherapy Centre. Cloth. Pp. 482, with some illustrations. Price, $14.75. E &. S. Livingstone Ltd., Edinburgh and London. Exclusive U. S. agents, The Williams & Wilkins Company, Baltimore, Md. 21202, 1968.

CLINICAL NUCLEAR MEDICINE. By C. Douglas Maynard, M.D., Assistant Professor of Radiology, Associate in Neurology, The Bowman Gray School of Medicine, Wake Forest University; Director of Nuclear Medicine, North Carolina Baptist Hospital, Winston-Salem, N. C. Cloth. Pp. 280, with 353 illustrations. Price, $12.50. Lea & Febiger, 600 Washington Square, Philadelphia, Pa. 19106, 1969.

COMPARATIVE STUDY OF ROENTGEN DIAGNOSTIC CLASSIFICATIONS: Computer Analysis of 124,496 Roentgen Reports. Acta Radiologica Supplementum 285. By Erkki Koivisto, Department of Radiology, University of Oulu, Finland. Paper. Pp. 126. Price, Sw. Kr. 35. Acta Radiologica, Stockholm 2, Sweden, 1969.

MALFORMATIONS OF THE INNER EAR IN DEAF CHILDREN: A Tomographic and Clinical Study. Acta Radiologica Supplementum 286. By Jorgen Jensen, Department of Diagnostic Radiology, Rigs-

hospitalet, Copenhagen, Denmark. Paper. Pp. 95, with some illustrations. Price, Sw. Kr. 35:-. Acta Radiologica, Stockholm 2, Sweden, 1969.

Radiotherapy and TNM Classification of Cancer of the Larynx: A Study Based on 1447 Cases Seen at the Radiotherapy Clinic of Helsinki During 1936–1961. Acta Radiologica Supplementum 287. By Pentti J. Taskinen. Paper. Pp. 121. Price, Sw. Kr. 35:-. Acta Radiologica, Stockholm 2, Sweden, 1969.

Arteries and Veins of the Human Brain. By Roger B. Stephens, Ph.D., M.D., Stanford University School of Medicine, Stanford, Calif.; and Donald L. Stilwell, M.D., Associate Professor of Anatomy, Stanford University School of Medicine, Stanford, Calif. Cloth. Pp. 180, with many illustrations. Price, $21.00. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62703, 1969.

Patient Care and Special Procedures in Radiologic Technology. Third edition. By John C. Watson, R. T., Technical Consultant, Department of Radiology, Yale Medical Center and Yale-New Haven Hospital, New Haven, Conn.; formerly, Director of Courses in X-Ray Technology, Minneapolis, Minn. Cloth. Pp. 234, with many illustrations. Price, $8.25. C. V. Mosby Company, 3207 Washington Blvd., St. Louis, Mo. 63103, 1969.

La Letteratura Radiologica Italiana. Volume XIII. Indice bibliografico dei lavori italiani di Radiologia degli anni 1965, 1966, 1967. Compiled by I. Belli, A. Caresano and L. A. de Santis. Paper. Pp. 386. La Tipografica Varese, Via Tonale, 49-Varese, Italy, 1969.

A Textbook of Radiology. Edited by David Sutton, M.D., F.R.C.P., F.F.R., Director, Radiological Department, St. Mary's Hospital, London W 2; Consultant Radiologist, Maida Vale Hospital (the National Hospitals for Nervous Disorders), London W 9; Teacher in Radiology, St. Mary's Hospital Medical School, University of London, and Institute of Neurology, University of London: assisted by Ronald G. Grainger, M.D., M.P.C.P., D.M.R.D., F.F.R., Consultant Radiologist to United Sheffield Hospitals; Consultant Radiologist in Charge, Northern General Hospital, Sheffield 5; Consultant Radiologist to Sheffield Cardio-Thoracic Centre, Sheffield; Clinical. Teacher in Radiology, University of Sheffield. Cloth. Pp. 1,186, with many illustrations. Price $42.50. E. & S. Livingstone Ltd., Edinburgh and London. Exclusive U. S. agents, The Williams & Wilkins Company, Baltimore, Md. 21202, 1969.

SOCIETY PROCEEDINGS

MEETINGS OF RADIOLOGICAL SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. Ted F. Leigh, Emory University Clinic, Atlanta, Ga. 30322. Annual Meeting: Washington-Hilton Hotel, Washington, D. C., September 30–October 3, 1969.

American Radium Society
Secretary, Dr. John V. Blady, The Parkway House, 2201 Benjamin Franklin Parkway, Philadelphia, Pa. 19130. Annual meeting: Hotel Coronado, San Diego, Calif., March 1–6, 1970.

Radiological Society of North America
Secretary-Treasurer, Dr. Maurice Doyle Frazer, 1744 South Fifty-eighth St., Lincoln, Neb. Annual meeting: Palmer House, Chicago, Ill., November 30–December 5, 1969.

American College of Radiology
Executive Director, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Ill. Annual meeting: Statler-Hilton Hotel, Dallas, Tex., March 31–April 4, 1970.

Section on Radiology, American Medical Association
Secretary, Dr. Kenneth L. Krabbenhoft, Harper Hospital, Detroit, Mich. 48201. Annual meeting: New York, N. Y., July 13–17, 1969.

American Board of Radiology
Secretary, Dr. C. Allen Good. Correspondence should be directed to Kahler Center Building, Rochester, Minn. 55901.
The oral examination will be held at the Statler Hilton Hotel, Dallas, Texas, Dec. 8–12, inclusive, 1969.
The deadline for filing applications for the above examination was December 31, 1968.

American Association of Physicists in Medicine
Secretary, Leonard Stanton, Hahnemann Medical College, 230 N. Broad St., Philadelphia, Pa. 19102.

American Society of Therapeutic Radiologists
Secretary, Dr. Carl R. Bogardus, Jr., University of Oklahoma Medical Center, Oklahoma City, Oklahoma 73104

American Society for Diagnostic Ultrasound
Secretary, Dr. Charles C. Grossman, 552 N. Neville St., Pittsburgh, Pa. 15213.

American Society of Neuroradiology
Secretary-Treasurer, Dr. Eugene V. Leslie, Edward J. Meyer Memorial Hospital, 462 Grider St., Buffalo, N. Y. 14215. Annual Meeting: Washington-Hilton Hotel, Washington, D. C., February 12 and 13, 1970.

Twelfth International Congress of Radiology
President, Dr. Kempo Tsukamoto, 9-1, 4-chome, Angewa, Chiba, Japan. Meeting: Hotel New Otani, Tokyo, Japan, Oct. 6–11, 1969.

Tenth Inter-American Congress of Radiology
Counselor for the United States, Dr. Juan A. del Regato, Penrose Cancer Hospital, 2215 North Cascade Ave., Colorado Springs, Colo. 80907.
President, Dr. Juan A. del Regato, Colorado Springs, Colo., USA.
Secretary, Dr. F. Bloedorn, Boston, Mass., USA.
Meeting: San Juan, Puerto Rico, 1971.

Inter-American College of Radiology
President, Dr. Oscar Soto, H. Urteaga 480, Lima, Perú.

Alabama Radiological Society
Secretary, Dr. William V. Weldon, Medical Arts Building, Birmingham, Ala. 35205. Meets time and place of Alabama State Medical Association.

Alaska Radiological Society
Secretary, Dr. Bruce C. Wright, Providence Hospital, Anchorage, Alaska. Meets third Wednesday each month.

Arizona Radiological Society
Secretary-Treasurer, Dr. Robert E. Steyskal, 550 W. Thomas Rd., Phoenix, Ariz. 85013. Two regular meetings a year. Annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Chapter of American College of Radiology
Secretary-Treasurer, Dr. Wilma C. Diner, Univ. of Arkansas Medical Center, Little Rock, Ark. 72201.

Arkansas Radiological Society
Secretary, Dr. Charles W. Anderson, 1108½ Poplar, Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Association of University Radiologists
Secretary-Treasurer, Dr. James J. Scatliff, University of North Carolina Medical School, Chapel Hill, N. C. 27514. Annual Meeting: University of Kentucky Medical Center, Lexington, Kentucky, April 29–May 1, 1970.

Atlanta Radiological Society
Secretary, Dr. Donald R. Rooney, Burnt Hickory Road, Marietta, Ga. Meets monthly except during three summer months, on third Tuesday, at the Academy of Medicine, Atlanta, Ga., at 8:00 P.M.

Bavarian-American Radiologic Society
Advisor, Colonel Paul E. Sieber. *Secretary*, Major Peter B. Riesz, USAH Bad Cannstatt, APO 09154, New York. N. Y. Meets quarterly.

Blockley Radiological Society
Secretary-Treasurer, Dr. R. John Gould, 41 Lombardy Rd., Drexel Hill, Pa. 19026.

Bluegrass Radiological Society
Secretary-Treasurer, Joseph A. Sayeg, Ph.D., Radiation Physicist, University of Kentucky, Lexington, Kentucky 40506. The Society meets once each month during the school year.

Brooklyn Radiological Society
Secretary, Dr. Coleman H. Rosenberg, 81–10 Chevy Chase St., Jamaica, N. Y. 11432. Meets first Thursday of each month, October through June.

Buffalo Radiological Society
Secretary, Dr. Herbert Pirson, 145 High Park Blvd., Buffalo, N. Y. 14226. Meets second Monday evening each month, October to May inclusive, at University Club.

California Radiological Society
Secretary-Treasurer: Dr. Leroy K. Mills, 3157 Oakcliff Circle, Carmichel, Calif. 95608. Meets annually during meeting of California Medical Association.

Catawba Valley Radiological Society
Secretary, Dr. Emmett R. White, P. O. Box 303, Rutherford College, N. C. 28671. Meets every Friday, Dept. of Radiology, Valdese General Hosp., Valdese, N. C., at 12:00 noon.

Central New York Radiological Society
Secretary-Treasurer, Dr. David N. Cheris, Community General Hospital of Greater Syracuse, Broad Road, Syracuse, N. Y. 13215. Meets first Monday each month, October through May.

Central Ohio Radiological Society
Secretary, Dr. Ollie E. Southard, 2787 Tudor Rd., Columbus, O. 43209. Meets second Thursday in October, November, January, and March 15 and May 19 at Fort Hayes Hotel, Columbus, Ohio.

*** Secretaries of societies are requested to send timely information promptly to the Editor.**

Chicago Roentgen Society
Secretary-Treasurer, Dr. Howard C. Burkhead, 2650 Ridge Ave., Evanston, Ill. 60202. Meets third Wednesday of each month, October to April, except December, at the University Club of Chicago.

Cleveland Radiological Society
Secretary-Treasurer, Dr. James Farmer, 18869 Canyon Rd. Fairview Park, Ohio 44126. Meetings at 7:00 P.M. on fourth Monday of October, November, January, February, March and April.

Colorado Radiological Society
Secretary, Dr. Charles E. Seibert, Department of Radiology, Swedish Hospital, 501 E. Hampton, Englewood, Colo. 80110. Meets third Friday of each month at Denver Athletic Club from September through May.

Connecticut Valley Radiologic Society
Secretary, Dr. William W. Walthall, Jr., 130 Maple St., Springfield, Mass. Meets in April and October.

Dallas-Fort Worth Radiological Society
Secretary-Treasurer, Dr. R. W. Perrin, P.O. Box 5999, Dallas, Texas 75222. Meets the 3rd Monday of every month at 6:30 P.M., at the Cibola Inn, Arlington, Texas.

Detroit Roentgen Ray Society
Secretary, Dr. David P. Corbett, Harper Hospital, Detroit, Mich. 48201. Meets monthly, first Thursday, October through May, at David Whitney House, 1010 Antietam, at 6:30 P.M.

East Bay Radiological Society
Secretary, Dr. Burke L. Winget, Samuel Merritt Hospital, 34th Webster Street, Oakland, Calif. 94609. Meets first Thursday each month, Oct. through May, at University Club, Oakland, Calif.

East Tennessee Radiological Society
Secretary-Treasurer, Dr. Eberhard F. Besemann, Baroness Erlanger Hospital, Chattanooga, Tenn. 37403. Meets in January and September.

Florida Radiological Society
Secretary, Dr. Robert H. Nickau, Good Samaritan Hospital, West Palm Beach, Fla. 33402. Meets twice annually, in the spring with the annual State Society Meeting and in the fall.

Florida West Coast Radiological Society
Secretary-Treasurer, Dr. Allen L. Sheer, University Community Hospital, 13505 N. 31st St., Tampa, Fla. 33612. Meets in January, March, May, July, September and November.

Georgia Radiological Society
Chapter of the American College of Radiology
Secretary, Dr. Walker Harris, The Medical Center, Columbus, Georgia 31902. Meets in spring and fall at Annual State Society Meeting.

Greater Cincinnati Radiological Society
Secretary-Treasurer, Dr. Owen L. Brown, 2421 Auburn Ave., Cincinnati, Ohio 45219.

Greater Louisville Radiological Society
Secretary-Treasurer, Dr. L. D. LeNeave, 315 E. Broadway, Louisville, Ky. 40202. Meets monthly.

Greater Miami Radiological Society
Secretary-Treasurer, Dr. Sylvan H. Sarasohn, P. O. Box 1256, North Miami, Fla. 33161. Meets monthly, third Wednesday at 8:00 P.M. at Jackson Memorial Hospital, Miami, Fla.

Greater St. Louis Society of Radiologists
Secretary-Treasurer, Dr. Roland P. Ernst, 3720 Washington Ave., St. Louis, Mo. 63108.

Hawaii Radiological Society
Secretary-Treasurer, Dr. Thomas C. Brown, 1697 Ala Moana Blvd., Honolulu, Hawaii 96815. Meets third Monday of each month at 7:30 P.M.

Health Physics Society
Secretary, R. J. Augustine, National Center for Radiologic Health, 1901 Chapman Ave., Rockville Md. 20852.

Houston Radiological Society
Secretary, Dr. Eleanor Montague, 6516 Bertner, Houston, Tex. 77025. Meets fourth Monday of each month, except June, July, August and December, at 6:00 P.M., at 103 Jesse H. Jones Library Building, Texas Medical Center, Houston, Tex. 77025.

Idaho State Radiological Society
Secretary, Dr. George H. Harris, Bannock Memorial Hospital, Pocatello, Idaho. Meets in the spring and fall.

Illinois Radiological Society, Inc.
Secretary, Dr. C. R. Markivee, 674 North Seminary St., Galesburg, Ill. 61401. Meets in the spring and fall.

Indiana Roentgen Society, Inc.
Secretary, Dr. Edwin F. Koch, Jr., 915 University Ave., Muncie, Ind. 47303. Meets first Sunday in May and during fall meeting of Indiana State Medical Association.

Iowa Radiological Society
Secretary-Treasurer, Dr. J. H. Lohnes, 1948 First Ave., N.E., Cedar Rapids, Iowa 52402. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

Kansas Radiological Society
Secretary-Treasurer, Dr. Robert C. Lawson, 310 Medical Arts Bldg., 10th and Horne, Topeka, Kan. Meets in spring with State Medical Society and in winter on call.

Kentucky Chapter, American College of Radiology
Secretary-Treasurer, Dr. Ralph C. Quillin, 1221 S. Broadway, Lexington, Ky. 40504. Meets in April and September.

Kings County Radiological Society
Secretary, Dr. Sidney Hendler, 1880 Ocean Ave., Brooklyn 30, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Knoxville Radiological Society
Secretary, Dr. Clifford L. Walton, Blount Professional Bldg., Knoxville 20, Tenn. Meetings are held the third Monday of every other month at the University of Tennessee Memorial Research Center and Hospital.

Long Island Radiological Society
Secretary, Dr. Robert J. Hochstim, 1200 Stewart Ave., Garden City, N. Y. 11533. Meets monthly.

Los Angeles Radiological Society
Secretary, Dr. John L. Gwinn, Childrens Hospital of Los Angeles, 4650 Sunset Blvd., Los Angeles, Calif. 90027. Meets second Wednesday of month in September, November, January, April and June at Los Angeles County Medical Association Building, Los Angeles, Calif.

Louisiana-Texas Gulf Coast Radiological Society
Secretary-Treasurer, Dr. Edward A. Sheldon, 109 Doctors Bldg., Beaumont, Texas 77701.

Maine Radiological Society
Secretary-Treasurer, Dr. Robert A. Bearor, Maine Medical Center, Portland, Maine 04102. Meets in June, September, December and April.

Maryland Radiological Society
Secretary, Dr. Nathan Stofberg, 4519 Hawksbury Rd., Pikesville, Md. 21208.

Massachusetts Radiological Society
Secretary, Dr. Jerome H. Shapiro, Department of Radiology, Boston City Hospital, 818 Harrison Ave., Boston, Mass. 02118.

Memphis Roentgen Society
Secretary-Treasurer, Dr. Webster Riggs, Jr., The University of Tennessee College of Medicine, Department of Radiology, Walter F. Chandler Bldg., 865 Jefferson Ave., Memphis, Tenn. 38103. Meets first Monday of each month at John Gaston Hospital.

Miami Valley Radiological Society
Secretary, Dr. Darwood B. Hance, Reid Memorial Hospital, Richmond, Indiana. Meets third Thursday of fall, winter and spring months at 7:30 P.M. at Miami Valley Hospital, Dayton, Ohio.

Mid-Hudson Radiological Society
Secretary-Treasurer, Dr. Herbert S. Berlin, Hopewell Junction, N. Y. Meets 7:00 P.M., first Wednesday of each month, September to May.

Milwaukee Roentgen Ray Society
Secretary-Treasurer, Dr. James E. Bell, 8700 W. Wiscon-

sin Ave., Milwaukee, Wis. 53213. Meets monthly on fourth Monday, October through May, at University Club.

Minnesota Radiological Society
Secretary-Treasurer, Dr. Warren L. Kump, 4243 Glenwood Ave., Minneapolis, Minn. 55422. Meets twice annually, fall and winter.

Mississippi Radiological Society
Secretary-Treasurer, Dr. Ottis G. Ball, 5356 Balmoral Drive, Jackson, Miss. 39211. Meets third Thursday of each month at the Heidelberg Hotel, Jackson, at 6:00 P.M.

Missouri Radiological Society
Secretary-Treasurer, Dr. Arthur A. Porporis, 100 N. Euclid Ave., St. Louis, Mo. 63108.

Montana Radiological Society
Secretary, Dr. Colvin H. Agnew, Doctors' Building, 1231 N. 29th Street, Billings, Montana 59101. Meets in Glacier National Park, July 23–25, 1969.

Nebraska State Radiological Society
Secretary-Treasurer, Dr. Otto A. Troester, 924 Sharp Building, Lincoln, Nebraska 60508. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

Nevada Radiological Society
Secretary, Dr. William G. Arbonies, Department of Radiology, St. Mary's Hospital, Reno, Nev.

New England Roentgen Ray Society
Secretary, Dr. Morris Simon, 330 Brookline Ave., Boston, Mass. 02115. Meets third Friday of each month, October through May, at The Longwood Towers, 20 Chapel Street, Brookline, Mass., at 4:30 P.M.

New Hampshire Roentgen Ray Society
Secretary, Dr. Paul Y. Hasserjian, 1470 Elm St., Manchester, N. H. Meets four to six times yearly.

New Mexico Association of Radiologists
Secretary-Treasurer, Dr. Justin J. Wolfson, Department of Radiology, Bernalillo County-Indian Hospital, Albuquerque, New Mexico.

New Mexico Society of Radiologists
Secretary, Dr. Donald A. Wolfel, Albuquerque, New Mexico. Four meetings annually, three held in Albuquerque, N. M., and one held at time and place of New Mexico State Medical Society annual meeting.

New York Roentgen Society
Secretary-Treasurer, Dr. Samuel H. Madell, 1 E. 82nd St New York, N. Y. 10024. Meets monthly on third Monday at the New York Academy of Medicine at 4:30 P.M.

New York State Chapter of the American College of Radiology, Inc.
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester, N. Y., 14618.

North Carolina Chapter of ACR.
Secretary-Treasurer, Dr. James F. Martin, 300 S. Hawthorne Road, Winston-Salem, N.C. 27103.

North Carolina Radiological Society
Secretary, Dr. E. H. Schultz, North Carolina Memorial Hospital, Chapel Hill, N. C. Meets in the spring and fall each year.

North Dakota Radiological Society
Secretary, Dr. A. Ohrt, 408 Medical Arts Bldg., Fargo, N. D. 58102. Meets at time of State Medical Association meeting. Other meetings arranged on call of the President.

North Florida Radiological Society
Secretary, Dr. Charles H. Newell, 800 Miami Road, Jacksonville 7, Fla. Meets quarterly in March, June, September and December.

Northeastern New York Radiological Society
Secretary, Dr. Herbert F. Reilly, Jr., 12 Sandalwood Rd., Scotia, New York 12302. Meets in Albany area on third Wednesday of October, November, March, April, and May.

Northern California Radiological Society
Secretary-Treasurer, Dr. Jean Romer, 1229 El Toro Way, Sacramento, Calif. 95825. Meets fourth Monday of Sept., Nov., Jan., March and May at Aldo's Restaurant in Sacramento.

Northwestern Ohio Radiological Society
Secretary, Dr. Vito J. Zupa, Mercy Hospital, Department of Radiology, Toledo, Ohio.

Ohio State Radiological Society
Secretary, Dr. Joseph Hanson, 1544 South Byrne Road, Toledo, Ohio 43614.

Oklahoma State Radiological Society
Secretary, Dr. Donald F. Mauritson, 100 Utica Square Med. Center, Tulsa, Okla. 74114. Meets in January, May and October.

Orange County Radiological Society
Secretary, Dr. Richard Simpson, Hoag Memorial Hospital, 301 Newport Ave., Newport Beach, California. Meets on fourth Tuesday of the month, excluding June, July, August, and December, at the Orange County Medical Association Bldg., Orange, Calif.

Oregon Radiological Society
Secretary-Treasurer, Dr. Clinton B. Sayler, 214 Medical Dental Bldg., Portland, Oregon 97205. Meets on second Wednesday of month, October through April, at the University Club, Portland, Ore.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans, La. 70113. Meets second Tuesday of each month.

Pacific Northwest Radiological Society
Secretary-Treasurer, Dr. Marvin Wallace, 555 108th Ave. N. E., Bellevue, Washington 98004.

Pennsylvania Radiological Society
Secretary, Dr. Theodore A. Tristan, Harrisburg, Polyclinic Hosp., Harrisburg, Pa. 17105.

Philadelphia Roentgen Ray Society
Secretary, Dr. C. Jules Rominger, Misericordia Hospital, 54th St. and Cedar Ave., Philadelphia, Pa. 19143. Meets first Thursday of each month at 5 P.M., from October to May in Thompson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. Norman Williams, Department of Radiotherapy, Montefiore Hospital, 3459 Fifth Ave., Pittsburgh Pa. 15213. Meets second Wednesday of month, October through June, at Park Schenley Restaurant.

Radiation Research Society
Secretary-Treasurer, Dr. Gail D. Adams, Dept. of Radiology, Univ. of Oklahoma Medical Center, Oklahoma City, Oklahoma 73104.

Radiological Society of Connecticut, Inc.
Secretary-Treasurer. Dr. Henry J. Fox, 10 Washington Ave., Bridgeport, Conn. Meetings are held quarterly.

Radiological Society of Greater Cincinnati
Secretary-Treasurer, Dr. Donald E. Gunderson, 3553 Bayard Dr., Cincinnati, Ohio 45208. Meets first Monday of each month at Cincinnati Academy of Medicine.

Radiological Society of Greater Kansas City
Secretary, Dr. Leo G. Goertz, 155 S. 18th St., Kansas City, Kans. 66102. Meets last Friday of each month.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Radiological Society of Louisiana
Secretary, Dr. Lester W. Eavenson, 2700 Napoleon Ave., New Orleans 15, La. Meets semiannually, during Louisiana State Medical Society meeting and 6 months later.

Radiological Society of New Jersey
Secretary, Dr. John W. Marquis, 12 Hawthorne Ave., East Orange, N. J. 07018. Meets in Atlantic City at time of State Medical Society meeting and in October or November in Newark, N. J.

Radiological Society of Rhode Island
Secretary-Treasurer, Dr. David R. Hallman, The Memorial Hospital, Pawtucket, R. I. 02860.

Radiological Society of South Dakota
Secretary-Treasurer, Dr. Donald J. Peik, 303 S. Minnesota Ave., Sioux Falls, S. D.

Radiological Society of Southern California
Secretary-Treasurer, Dr. Robert G. Williams, The Santa Barbara Medical Clinic, P.O. Box 1200, Santa Barbara, Calif. 93102. Meets three times a year, usually October, February and May.

Radiological Society of the State of New York
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester, N. Y. 14618.

Redwood Empire Radiological Society
Secretary, Dr. Lee F. Titus, 164 W. Napa St., Sonoma, Calif. Meets second Monday every other month.

Richmond County Radiological Society
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga. Meets first Thursday of each month at various hospitals.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Kenneth E. Robinson, Rochester General Hospital, 1425 Portland Ave., Rochester, N. Y. 14621. Quarterly meetings on the call of the President, at the Rochester Academy of Medicine.

Rocky Mountain Radiological Society
Secretary-Treasurer, Dr. Robert W. Lackey, 4200 E. Ninth Ave., Denver, Colo. 80220. Annual meeting: Brown Palace Hotel, Denver, Colo., Aug. 21–23, 1969.

San Antonio-Civilian-Military Radiological Society
Secretary, Dr. Lee F. Rogers, Department of Radiotherapy, Bexar County Teaching Hospital, 4502 Medical Drive, San Antonio, Texas. Meets third Wednesday of each month at Fort Sam Houston Officers' Club at 6:30 P.M.

San Diego Radiological Society
President-Secretary, Charles R. Henkelmann, 3909 Palm Drive, Bonita, Calif. 92002. Meets first Wednesday of each month at the Town & Country Motel.

San Francisco Radiological Society
Secretary-Treasurer, Dr. Warren M. Russell, Franklin Hospital, Castro & Duboce, San Francisco, Calif. 94114. Meets quarterly at various hospitals (contact Secretary).

Santa Clara County Radiological Society
Secretary, Dr. John J. Berg, 45 So. 17th Street, San Jose, Calif. 95112. Meets monthly at the Santa Clara County Medical Association Bldg., 700 Empey Way, San Jose, Calif.

Section on Radiology, California Medical Association
Secretary, Dr. William H. Graham, 630 East Santa Clara St., San Jose, Calif.

Section on Radiology, Medical Society of the District of Columbia
Secretary-Treasurer, Dr. Louis Wener, Cafritz Memorial Hosp., 1310 Southern Ave., S.E., Washington, D. C. 20032. Meets at Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

Section on Radiology, Southern Medical Association
Secretary, Dr. Phillip W. Voltz, Jr., 120 Medical Professional Bldg., San Antonio, Texas 78212. Annual meeting: To be announced.

Section on Radiology, Texas Medical Association
Secretary, Dr. George F. Crawford, St. Elizabeth Hospital, Beaumont, Tex. Meets annually with the Texas Medical Association.

Shreveport Radiological Club
Secretary, Dr. W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday at 7:30 P.M., September to May inclusive.

Society for Pediatric Radiology
Secretary, Dr. John L. Gwinn, Children's Hospital, 4614 Sunset Blvd., Los Angeles 27, Calif. Annual meeting: Washington-Hilton Hotel, Washington, D.C., September 29, 1969.

Society of Nuclear Medicine
Secretary, Mr. C. Craig Harris, Oak Ridge National Laboratories, Oak Ridge, Tenn. *Administrator*, Mr. Samuel N. Turiel, 430 N. Michigan Ave., Chicago 11, Ill.

South Bay Radiological Society
Secretary, Dr. Emerson C. Curtis, University Dr., Menlo Park, Calif. 94025. Meets second Wednesday of each month.

South Carolina Radiological Society
Secretary, Dr. George W. Brunson, 1406 Gregg St., Columbia, S. C. Annual meeting (primarily business) in conjunction with the South Carolina Medical Association meeting in May. Annual fall scientific meeting at time and place designated by the president.

South Dakota Radiological Society
Secretary, Dr. Donald J. Peik, 1417 S. Minnesota Ave., Sioux Falls, S. Dak. Meets in spring with State Medical Society and in fall.

Southern California Radiation Therapy Society
Secretary-Treasurer, Dr. Aaron G. Fingerhut, 1000 W. Carson St., Torrance, Calif. 90502. Meets quarterly.

Southern Radiological Conference
Secretary-Treasurer, Dr. Marshall Eskridge, Mobile Infirmary, P.O. Box 4097, Mobile, Ala. 36604. Annual meeting: Grand Hotel, Pointe Clear, Ala. 36564, Jan. 30–Feb. 1, 1970.

Southwestern Radiological Society
Secretary, John M. McGuire, 904 Chelsea, El Paso, Tex. Meets last Monday of each month at 6:30 P.M. in the Paso del Norte Hotel.

Tennessee Radiological Society
Secretary-Treasurer, Dr. Lawrence R. Nickell, Maury County Hospital, Columbia, Tennessee 38401. Meets annually at the time and place of the Tennessee State Medical Association meeting.

Texas Radiological Society
Secretary, Dr. Herman C. Schested, 815 Medical Arts Bldg., Fort Worth 2, Tex. Annual meeting to be announced.

Tri-State Radiological Society
Secretary, Dr. John H. Marchand, Jr., Methodist Hospital, Henderson, Ky. Meets third Wednesday of Oct., Jan., March and May, 8:00 P.M., Elks Club in Evansville, Ind.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital, Ann Arbor Mich.

Upper Peninsula Radiological Society
Secretary, Dr. A. Gonty, Menominee, Mich. Meets quarterly.

Utah State Radiological Society
Secretary-Treasurer, Dr. Leon M. Neal, St. Benedict's Hospital, 3000 Polk Ave., Ogden, Utah 84403. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

Vermont Radiological Society
Secretary, Dr. John R. Williams, 160 Allen St., Rutland, Vt.

Virginia Radiological Society
Secretary-Treasurer, Dr. K. Kenneth Wallace, Jr., Virginia Beach, Va.

Washington State Radiological Society
Secretary-Treasurer, Dr. Paul S. Paulson, 1001 Broadway, Seattle, Washington 98122. Meets quarterly.

West Virginia Radiological Society
Secretary-Treasurer, Dr. George G. Green, Department of Radiology, W. Va. Univ. Medical Center, Morgantown, W. Va. 26506. Meets concurrently with Annual Meeting of West Virginia State Medical Society; other meetings arranged by program committee.

Westchester County Radiological Society
Secretary, Dr. Edgar Palmer, 650 Main St., New Rochelle, N. Y. 10801.

Meets on third Tuesday of January and October and on two other dates.

Wisconsin Radiological Society
Secretary-Treasurer, Dr. Robert E. Douglas, 117 N. Commercial St., Neenah, Wis. 54956. Meets twice a year, May and September.

Wyoming Radiological Society
Secretary, Dr. J. D. Grant, Memorial Hosp., Sheridan, Wyo. Meets in fall with State Medical Society and in spring on call of President.

Mexico, Puerto Rico and Central America

Asociación Costariccense de Radiología
Secretary, Dr. Jorge Vargas Segura, Apartado 5367, San José, Costa Rica.

Asociación de Radiólogos de Centro America y Panamá. Comprising: Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica and Panamá.
Secretary-General, Dr. Roberto Calderón, Calle Central Oeste No. 218, Managua, Nicaragua, Central America. Meets annually in a rotating manner in the six countries.

Sociedad de Radiología de El Salvador
Secretary, Dr. Julio Astacio, 5a Av. Nte. No. 434, San Salvador, Rep. El Salvador.

Sociedad de Radiología de Guatemala
Secretary, Dr. Carlos E. Escobar, 9ª. Calle A 0-05, Zona 1, Guatemala.

Sociedad Mexicana de Radiología, A.C.
Coahuila No. 35, México 7, D. F.
Secretary-General, Dr. Ramón Ruenes.
Meets first Monday of each month.

Asociación Puertorriqueña de Radiología
Secretary, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, Puerto Rico.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sánchez, Apartado No. 6323, Panamá, R. de P. Meets monthly in a department of radiology of a local hospital chosen at preceding meeting.

Sociedad Radiológica de Puerto Rico
Secretary, Dr. Felipe N. de Jesús, Apt. 9387, Santurce, Puerto Rico. Meets second Thursday of each month at 8:00 P.M. at the Puerto Rico Medical Association Bldg. in San Juan.

British Commonwealth of Nations

Association of Radiologists of the Province of Quebec
Secretary, Dr. R. Robillard, Notre-Dame Hospital, 1560 Sherbrooke St., East, Montreal, Que., Canada. Meets four times a year.

British Institute of Radiology
Honorary Secretary, Dr. G. H. du Boulay, 32 Welbeck St., London, W. 1, England. Meets monthly from October until May.

Canadian Association of Physicists, Division of Medical and Biological Physics.
Honorary Secretary-Treasurer, Paul M. Pfalzner, Department of Therapeutic Radiology, University of Western Ontario, London, Ontario, Canada.

Edmonton and District Radiological Society
Secretary, J. D. R. Miller, M.B., University of Alberta Hospital, Edmonton, Alberta, Canada. Meets third Thursday of each month October to May, except December, at various Edmonton Hospitals.

Faculty of Radiologists
Honorary Secretary, Dr. J. N. Pattinson, 47 Lincoln's Inn Fields, London, W.C.2, England.

Faculty of Radiologists, Royal College of Surgeons in Ireland
Registrar, Dr. H. O'Flanagan, F.R.C.P.I., D.P.H., 123 St. Stephens Green, Dublin 2, Ireland.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1, England.

Canadian Association of Radiologists
Honorary Secretary-Treasurer, Dr. Maurice Dufresne, *Associate Honorary Secretary-Treasurer*, Dr. F. Robert MacDonald, 1555 Summerhill Ave., Montreal 25, Que., Canada. Annual Meeting: To be announced.

Montreal Radiological Study Club
Secretary, Dr. Leonard Rosenthall, Montreal General Hospital, Montreal, Que., Canada. Meets first Tuesday evening, October to April.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française de Radiologie
Secretary General, Dr. Guy Duckett, 1385 est, rue Jean Talon, Montréal P.Q., Canada. Meets every third Tuesday from October to April, Annual Meeting: Nov. 6–8, 1969.

Toronto Radiological Society
Secretary, Dr. George Wortzman, Toronto General Hosp., Toronto 12, Ont., Canada. Meets second Monday of each month, September through May.

College of Radiologists of Australasia
Honorary Secretary, Dr. T. P. Loneragan, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W., Australia.

South America

Asociación Argentina de Radiología
Secretary, Dr. Lidio G. Mosca, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

Ateneo de Radiologia
Secretary, Dr. Victor A. Añaños, Instituto de Radiologia, Santa Fe 3100, Rosario, Argentina. Meets monthly on second and fourth Fridays at 7:00 P.M. in the Hospital Nacional de Centenario, Santa Fe 1300, Rosario.

Colégio Brasileiro de Radiologia
Secretary-General, Dr. Miguel Mario Céntola, Caixa Postal 5984, São Paulo, Brazil.

Sociedad Argentina de Radiología
Secretary-General, Dr. Juan R. Heilbuth, Pacheco, Santa Fe 1171, Buenos Aires. Meets First Wednesday evening, April through December.

Sociedad Boliviana de Radiología
Secretary, Dr. Javier Prada Méndez Casilla 1182, La Paz, Bolivia. Meets monthly. General assembly once every two years.

Sociedade Brasileira de Radiologia
Secretary, Dr. Armando Rocha Amoêdo, Cxa Postal 1532, Rio de Janeiro, Brazil. General Assembly meets every two years in December.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Chilena de Radiología
Secretary, Dr. Manuel Concha, Casilla 13426, Santiago, Chile. Meets fourth Friday of each month.

Sociedad Colombiana de Radiologia
Secretary-General, Dr. Armando Uribe, Hospital Militar Central, Apartado aéreo No. 5804, Bogotá, Colombia. Meets last Thursday of each month.

Sociedad Ecuatoriana de Radiología y Fisioterapía
Secretary, Dr. Carlos Palau, Av. Bogotá 206, Guayaquil, Ecuador.

Sociedad Paraguaya de Radiología
Secretary, Dr. Miguel González Addone, 15 de Agosto 322, Asunción, Paraguay.

Sociedad Peruana de Radiologia
Secretary-General, Dra. Ladis Delpino, Instituto de Radiología "Cayetano Heredia" Hospital Arzobispo Loayza, Lima, Perú. Meets monthly except during January, February and March.

Sociedad de Radiologica del Atlantico
Secretary, Dr. Raul Fernandez, Calle 40 #41–110, Baran-

quilla, Colombia. Society meets monthly at the Instituto de Radiología.

Sociedad de Radiología, Cancerología y Física Médica del Uruguay
Secretary-General, Dr. José Claussius, Av. Agraciada 1464, piso 13, Montevideo, Uruguay.

Sociedade de Radiología de Pernambuco
Secretary, Dr. Manoel Medeiros, Instituto de Radiologia da Faculdade de Medicina da Universidade do Recife, Caixa Postal 505, Pernambuco, Brazil.

Sociedad de Roentgenología y Medicina Nuclear de la Provincia de Córdoba
Secretary-General, Dr. Lucas C. Di Rienzo, Ave. Grl. Paz. 151, Córdoba, Argentina.

Sociedad Venezolana de Radiología
Secretary-General, Dr. Modesto Rivero Gonzáles, Apartado No. 9362 Candelaria, Caracas, Venezuela. Meets monthly, third Friday at Colegio Médico del Distrito Federal, Caracas.

Continental Europe

Österreichische Röntgen-Gesellschaft
President, Dr. Konrad Weiss, Mariannengasse 10, Vienna 9, Austria. Meets second Tuesday of each month in Allgemeine Poliklinik.

Société Royale Belge de Radiologie
General Secretary, Dr. Joseph Baeyens, Alost, Belguim. Meets in February, March, May, June, September, October, November and December.

Société Européenne de Radiologie Pédiatrique
Permanent Secretary, Dr. Jaques Sauvegrain, Hôpital des Enfants-Malades, 149, rue de Sèvres, Paris 15e, France.
General Secretary, Dr. H. Ludin, Department of Roentgenology, Basler Kinderspital, Basel, Switzerland.

Société Française d'Electroradiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, du Nord, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord. Central Society meets third Monday of each month, except during July, August and September, rue de Seine 12, Paris, France.
Secretary-General, Dr. Ch. Proux, 9 rue Daru Paris 8e, France.

Československá Společnost pro Roentgenologii a Radiologii
Secretary, Dr. Robert Poch, Praha 12, Srobárova 50, Czechoslovakia. Meets monthly except during July, August and September. Annual general meeting.

Deutsche Röntgengesellschaft
President, Professor Dr. med. Hanno Poppe, Radiologische Univ.-Klinik, Gossler Str. 10, 34 Göttingen, Germany.

Società Italiana di Radiologia Medica e di Medicina Nucleare
Secretary, Dr. Ettore Conte, Ospedale Mauriziano Torino, Italy. Meets annually.

Nederlandse Vereniging voor Radiologie
Secretary, Dr. C. B. A. J. Puijlaert, Prof. Donderastraat 73, Tilburg, Netherlands.

Scandinavian Radiological Society
Secretary-General, Professor C. E. Unnérus, M.D., Hagalung-Tapiola, Havsvindsvägen 5 C., Finland.

Sociedad Española de Radiología y Electrología Médicas y de Medicina Nuclear
Secretary, Juan Gómez López, Villanueva, 11, Madrid 1. Meets every second Friday of each month, Oct. to June, inclusive, in Madrid.

Schweizerische Gesellschaft für Radiologie und Nuklearmedizin (Société Suisse de Radiologie et de Médecine Nucléaire)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

Asia

Indian Radiological Association
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

Indonesian Radiological Society
Secretary, Professor Sjahriar Rasad, Taman Tjut Mutiah I Diakarta, Indonesia

Iranian Radiological Society
Secretary, Dr. Issa Yaghmai, P.O. Box No. 14-1151, Teheran, Iran. The Society meets on the second Saturday of each month.

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ABSTRACTS OF RADIOLOGICAL LITERATURE

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ROENTGEN DIAGNOSIS

Head

Jochem, W., and Buchelt, L. Ein Fall einer Hirnembolie nach Lymphographie. (A case of cerebral embolism following lymphography.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, Nov., 1968, *109*, 585–586. (Address: Dr. W. Jochem, Universitäts-Strahlen-Klinik, Robert Koch Strasse, 355 Marburg, Germany.)

Lipoid microembolization of the lungs occurs normally when lymphangiography is performed. A superimposed lipoid pneumonia, however, represents a more serious complication and prevails mostly in patients with cardiopulmonary diseases. Serious cerebral symptoms are extremely rare and have been reported in only 2 instances out of 16,000 recorded lymphangiographies. A third case is described.

The patient was a woman, age 47, who had received radiotherapy for a fist-size parametrial recurrence of a cervical cancer. A unilateral hydronephrosis was also present. During the course of treatments, the patient had suffered a bout of pneumonia. Hematologic tests disclosed an anemia with 7 gm. per cent hemoglobin and a lymphopenia.

Lymphography was performed with 25 ml. lipiodol U.F. The speed of the injection was 0.1 ml./min. Pertinent lymphographic findings were an impeded flow in the left pelvic area and metastatic seeding in aortic lymph nodes. The same evening, the patient suddenly jumped out of her bed, then reclined and voided. During the same night, she proved restless, groggy and completely disoriented as to time and space. For the following 2 days she developed fever which responded well to antibiotic therapy. Neurologic manifestations suggested a disseminated cerebral process of a migratory nature with pyramidal tract symptoms on the right and, later on, sensibility disturbances on the left side. Symptoms of ataxia varied a great deal but disorientation and drowsiness remained constant. The electroencephalogram disclosed a severe acute cerebral dysfunction with marked delta activity. It improved only slightly although clinical manifestations completely disappeared within a period of 2 weeks.

The question of how the oil reached the cerebral circulation remains problematic. The amount of 10 ml. infused during a period of 120 minutes is small but in the course of events has proved excessive. Storage of contrast material in metastatically seeded lymph nodes is distinctly reduced. In the described case, the retroperitoneal space has further impeded the flow of lipiodol due to damage from radiotherapy and cytostatic medication. An intercurrent pneumonia may have reduced the effectiveness of pulmonary filtration. Thus, several factors could have contributed to the massive cerebral embolization.—*E. Kraft, M.D.*

Paulson, O. B., Cronqvist, S., Risberg, J., and Jeppesen, F. I. Regional cerebral blood flow: a comparison of 8-detector and 16-detector instrumentation. *NM, J. Nuclear Med.*, Apr., 1969, *10*, 164–173. (From: Bispebjerg Hospital, Copenhagen, Denmark and University Hospital, Lund, Sweden.)

Several investigators have studied regional cerebral blood flow, using an intra-arterial bolus of xenon 133, and employing a cluster of external scintillation probes. The appropriately collimated probes are attached to counting rate meters and the information is continuously displayed on a strip chart recorder.

The authors studied a group of 10 patients, 7 of whom had neoplasms and 3 of whom had cerebral vascular lesions. This group was studied with two instrument systems, one consisting of an 8-channel detector and the other of a 16-channel detector.

Two observations of importance were made: (1) It was found that only the first 2 minutes of the clearance curve needed to be studied for maximum information, rather than the 10 minute period originally recommended. The authors felt that the significant, assessible abnormalities such as shunt peak, tissue peak, and abnormal initial slope index were all contained within the shorter observation period, and that study of the 2 minute curve yielded better information than did study of the 10 minute curve. (2) The 16-detector system provided better resolution of all lesions than did the 8-detector unit, and 1 lesion identified with the 16-detector system was missed by the 8-detector unit.

The authors believe that a gamma camera, or any other detector which has a dead-time, is not suitable for appraisal of regional cerebral blood flow.—*Frederick J. Bonte, M.D.*

Neck and Chest

Debonnière, C., Carle, S., Bergiron, C., and Cioppani, F. La leishmaniose laryngée. (Laryngeal leishmaniasis.) *J. de radiol., d'électrol. et de méd. nucléaire*, Oct., 1968, *49*, 727–730. (From: Service Central d'Electroradiologie de Hôpital d'Instruction des Armées du-Val-de-Grâce, Paris, France.)

This case report concerns a 40 year old male who has spent the last 7 years of his army career overseas. After a period of commando training in the south of France, the patient noticed a 10 kg. loss of weight, progressive dysphonia, cough and mild fever. Laryngoscopic examination revealed extensive edema involving the epiglottis, aryepiglottic folds, ventricular folds and vocal cords. In addition to being thickened, the vocal cords were covered by grape-like nodular proliferations. In short, the laryngeal air-passages were narrowed and reduced to a tortuous stenosis. The piriform sinuses had lost their power

to expand. The lateral mobility of the larynx was diminished. The cervical lymph nodes were not enlarged. Anemia was noted (red blood cell count of 3,500,000) with leukopenia and increased monocytes (40 to 58 per cent).

Conventional roentgenograms and tomograms demonstrated a diffuse infiltration corroborating the endoscopic findings; the endo-laryngeal aspect of the epiglottis was covered by polypoid proliferations. The lumen of the ventricles was greatly reduced by the swelling of the ventricular and vocal folds. The right ventricle was almost totally obliterated by a nodule developing on the superior border of the vocal cord. The subglottic space was partially occupied by the edematous tracheal mucosa. Syphilis and tuberculosis being ruled out, the cancerous nature of the process appeared as most probable, although two biopsies were reported as showing only chronic inflammation.

Radiotherapy was then contemplated, but was postponed awaiting the report of a third biopsy. The histologic studies revealed reticulo-histiocytic infiltration of the submucosa with the cytoplasm of numerous cells loaded with Leishmania. The specific variety of the Leishmania could not be identified because the attempts at culture were unsuccessful. Treatment by antimony salts resulted in a rapid improvement in the patient's condition.

This case report illustrates that in the presence of a tumefaction of the larynx simulating cancer at first sight, it is necessary to bear in mind the possibility of inflammation caused by specific organisms, such as syphilis, tuberculosis, mycoses and even protozoa of the rarest kind.—*H. P. Lévesque, M.D.*

TURINA, M., SCHAMAUN, M., and WALDVOGEL, W. Crohn's disease of the oesophagus. *German Med. Monthly*, Feb., 1969, *14*, 49–50. (Address: Dr. M. Turina, Chirurgische Klinik, Kantonsspital, CH-7000 Chur, Switzerland.)

Crohn's disease in the esophagus has previously been reported in 1 case.

The authors present another in a 35 year old female who had had increasing difficulty in swallowing. A barium swallow examination showed an area of stenosis in the lower esophagus. This progressed to complete obstruction, necessitating surgery. Resection and anastomosis were performed.

Histologically, the characteristics of Crohn's disease were identified.—*George L. Sackett, Jr., M.D.*

PUSEY, V. A., MACPHERSON, R. I., and CHERNICK, V. Pulmonary fibroplasia following prolonged artificial ventilation of newborn infants. *Canad. M. A. J.*, Mar. 8, 1969, *100*, 451–457. (Address: Dr. V. Chernick, Children's Hospital, 685 Bannatyne, Winnipeg 3, Manitoba, Canada.)

Diffuse interstitial fibroplasia with associated proliferation of the bronchiolar endothelium has been proposed by Northway, Rosan, and Porter as representing a complication of oxygen toxicity superimposed upon the healing phase of hyaline membrane disease. The authors felt that these two conditions were not a prerequisite for the development of this complication.

They reviewed 51 neonatal cases of infants with respiratory distress, who had received artificial positive-pressure therapy in the intensive care unit of Children's Hospital.

From their analysis, the authors have shown that diffuse interstitial pulmonary fibroplasia may develop in infants without a history of hyaline membrane disease or high concentrations of oxygen therapy. They cited several other factors that may play a role in the development of this pulmonary abnormality, as well as recommending a plan of management for infants that require prolonged artificial ventilation.—*Victor G. Mikity, M.D.*

GAUTAM, H. P. Pulmonary angiography with external cardiac compression in fatal pulmonary embolism. *Brit. M. J.*, Nov. 23, 1968, *4*, 494–495. (From: Cardiothoracic Surgical Unit, Royal Infirmary, University of Manchester, Manchester, England.)

A case is reported of a male, age 38 years, admitted to the hospital for barbiturate poisoning. Two weeks after successful treatment by intermittent positive pressure ventilation and conventional medical therapy, he suddenly collapsed with cardiac arrest. He responded to external cardiac compression and other resuscitative measures. A presumptive diagnosis of pulmonary embolism was made. Selective pulmonary arteriography was performed while his circulation was artificially maintained. The study showed a block of the left lower lobe pulmonary artery.

Using peripheral supporter bypass, embolectomy was performed. However, the patient died approximately 1 hour after the surgery. The unsuccessful outcome was attributed to delayed surgery as it was about 2 hours after the cardiac arrest that the pulmonary obstruction was bypassed.

The author comments on the frequent difficulty in establishing a clinical diagnosis of pulmonary embolism and stresses the urgency of appropriate diagnostic procedures. The case emphasizes that a good diagnostic selective pulmonary angiogram may be obtained even when external cardiac compression is needed to support the circulation.—*Saul Heiser, M.D.*

CARRINGTON, CHARLES B., ADDINGTON, WHITNEY W., GOFF, ANNE M., MADOFF, IRVING M., MARKS, ASHER, SCHWABER, JULES R., and GAENSLER, EDWARD A. Chronic eosinophilic pneumonia. *New England J. Med.*,

Apr. 10, 1969, *280*, 787–798. (Address: Dr. E. A. Gaensler, The Thoracic Services, Boston University School of Medicine, 80 E. Concord Street, Boston, Mass. 02118.)

Nine women presented with a similar and distinctive syndrome consisting of a chronic and often life threatening illness with cough, high evening fever, night sweats, progressive dyspnea, 10–45 pound weight loss and deterioration on antituberculous therapy. Asthma occurred in 6 patients, whereas 3 had neither asthma nor blood eosinophilia.

The roentgenographic findings were unique, consisting of: (1) Progressive dense infiltrates arranged in a peripheral pattern—a "photographic negative or reversal" of the shadow seen in pulmonary edema or alveolar proteinosis; (2) surprisingly rapid resolution with corticosteroid therapy—evidence of clearing in 3–4 days and complete clearing within 1 month; and (3) recurrence of lesions in the same unusual pattern during relapse after corticosteroids had been withdrawn. The recurrence of pulmonary infiltrates identical in size, shape and location to those of the initial episdoe with clinical relapse also was striking and, in the authors' experience, unique.

The moderate to extensive consolidation noted grossly was due to leukocytic exudation into the interstitial tissues and small air spaces. Mature eosinophils were numerous and led to the description of: hronic eosinophilic pneumonia.

The differential diagnosis includes tuberculosis, but the patients markedly deteriorated on antituberculous therapy; sarcoidosis, although the pulmonic distribution was unusual for that disease; and Loeffler's pneumonia, however, as opposed to that often benign syndrome, this new entity showed progressive massive pulmonary infiltration and was highly symptomatic.

Because of the reliable clinical and roentgenographic findings, as well as the response to corticosteroids, the authors no longer require lung biopsy for diagnosis of "chronic eosinophilic pneumonia."—*Jerald B. Maltzman, M.D.*

Scadding, J. G. The lungs in rheumatoid arthritis. *Proc. Roy. Soc. Med.*, March, 1969, *62*, 227–238. (From: Institute of Diseases of the Chest, Brompton Hospital, London, England.)

The author distinguishes 3 different types of pulmonary involvement associated with rheumatoid arthritis.

He describes intrapulmonary nodules both in the Caplan type, and in patients without pneumoconiosis, having a histologic structure similar to that of subcutaneous rheumatoid nodules. These changes occur almost exclusively in patients with the clinical syndrome of rheumatoid arthritis, and they probably have a considerable overlap as causal factors with rheumatoid arthritis.

The author also states that pleural effusions in patients with rheumatoid arthritis may be associated with pleural or subpleural rheumatoid nodules and may have an unusually low glucose content. Pleural effusions during life and pleural adhesions at necropsy are significantly frequent in patients with rheumatoid arthritis. A relationship through common factors in pathogenesis is likely.

Fibrosing alveolitis of mural type occurs only rarely in patients with rheumatoid arthritis, but among patients with this sort of lung disease a proportion high enough to suggest more than a chance association also has rheumatoid arthritis.—*C. Peter Truog, M.D.*

Gregl, A., Eydt, M., Fernandez-Redó, E., Krack, U., and Yu, D. Lipiodol-Embolie nach Lymphographie (I. Klinischer Teil). (Lipiodol embolism following lymphography [I. Clinical part].) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, Nov., 1968, *109*, 575–585. (Address: Dr. A. Gregl, Oberarzt der Radiologischen Univ.-Klinik, Humboldtallee 10, 34 Göttingen, Germany.)

The authors report their experience with 906 lymphographies performed on 804 patients. In 34 per cent of the patients the temperature was elevated by 1°C., especially the day following the infusion. This phenomenon represents the natural result of each oil infusion. It is reversible and clears promptly without any special treatment.

Oil-embolism pneumonia (micro-fat embolism), on the other hand, represents a more serious complication. Such development usually occurs in patients with chronic pulmonary disease. Under these circumstances, the dose of contrast material has to be reduced. A quantity of 12 to 14 ml. proves adequate for the lower extremities but not for the para-aortic lymph nodes. No serious pulmonary involvement can be expected when the rate of injection is 1 ml./min. and when the infusion is made into an upper extremity instead of a lower one.

Reports of positive roentgen findings vary from 10 to 55 per cent. Actually, minute roentgen changes can be observed in all patients 10 to 24 hours following the infusion. A micromiliary spread is best recognized in the upper lung fields. Secondary pulmonary changes may develop after 3 or more days. Rapid infusion of at least 15 ml. of contrast material can result in an arborizing pulmonary embolization with a bronchogram-like effect. There is a marked discrepancy between the clinical and roentgen findings. Absent or transient meager clinical manifestations (dyspnea, cyanosis, hemoptysis) in spite of marked roentgenographic changes are pathognomonic for embolic lipiodol pneumonia.

Three cases with oil-embolism pneumonia are reported. The first patient was a 75 year old man with carcinoma of the urethra. In this case, the pulmonary

infiltration cleared within 7 days. The second patient was a 64 year old woman with the diagnosis of carcinoma of the sigmoid colon. Following the oil infusion, there was intermittent hemoptysis for 12 days and the temperature remained elevated for 10 days. Roentgenographic changes of the lungs cleared within a period of 3 weeks. The third patient was a 66 year old woman with a history of hypertension. Following the infusion, the temperature rose to 102°F. for 2 days but subsided with the aid of antibiotic medication. Five days following the infusion, marked bronchopneumonic changes were observed in the roentgenograms of the chest. Six days later, the roentgen findings became normal.—*E. Kraft, M.D.*

McMYN, J. K. Tetralogy of Fallot: angiocardiographic diagnosis compared with surgical findings. *Australasian Radiol.*, Feb., 1969, *13*, 37–73. (Address: Senior Radiologist, Green Lane Hospital, Auckland, New Zealand.)

This article consists of a very detailed analysis of 60 cases of the tetralogy of Fallot examined by angiocardiography and later subjected to surgery.

The angiographic and surgical findings are compared, and an attempt is made to catalogue the site and extent of the relevant lesions such as the pulmonary stenoses and ventricular septal defects in minute detail, all carefully tabulated.

The success of this attempt is such that a mass of information is available with appropriate case histories which, however, do not lend themselves to meaningful abstracting. It is recommended that those interested in the subject consult the original text.

The main subjects covered are: anatomy of the infundibular, valvular, and peripheral types of pulmonary stenoses; double outlet right ventricle; septal defects; and degree of over-ride of the aorta.—*Roger Pyle, M.D.*

CAMPEAU, LUCIEN, BOURASSA, MARTIAL G., BOIS, MARC A., SALTIEL, JACQUES, LESPÉRANCE, JACQUES, RICO, OSWALDO, DELCAN, JEAN-LOUIS, and TELLERIA, MOISE. Clinical significance of selective coronary cinearteriography. *Canad. M. A. J.*, Dec. 7, 1968, *99*, 1063–1068. (Address: Dr. Lucien Campeau, Department of Medicine, Institute of Cardiology of Montreal, 5000 Belanger Street East, Montreal 36, Quebec, Canada.)

The clinical and electrocardiographic findings were correlated with the findings obtained by selective coronary cinearteriography in 234 patients suspected of coronary disease.

Ninety-six per cent of the patients presumed not to have coronary insufficiency had no arteriographic evidence or significant obstructive coronary disease, whereas 80 per cent of patients complaining of typical angina had significant stenosis of 1 to 3 major coronary arteries. Patients with myocardial infarction showed 90.9 per cent incidence of significant obstructive coronary artery disease. Reduction of the lumen of at least 1 coronary artery by 50 per cent or more was almost regularly associated with angina or myocardial infarction. Less severe lesions and anomalies of the size and distribution not easily distinguishable from normal variants may be related to clinical and electrocardiographic findings of doubtful significance with less confidence and probably do not produce symptoms. A few patients with typical angina and rare cases of apparent myocardial infarction did not have significant arteriographic evidence of obstructive coronary disease.

It is believed that some patients may have angina pectoris due to a mechanism other than coronary arteriosclerosis. It is also postulated that rare cases of myocardial infarction may have normal arteriograms because of recanalization of a thrombus or other yet unknown causes. In patients without myocardial infarction, the correlation of the findings on coronary cinearteriography with resting electrocardiogram was of a lower order than that with the actual description of the chest pain; the latter appears to be definitely more indicative of angina pectoris.—*Saul Heiser, M.D.*

ABDOMEN

JAMES, W. B., and MELROSE, A. G. Metoclopramide in gastrointestinal radiology. *Clin. Radiol.*, Jan., 1969, *20*, 57–60. (From: The Southern General Hospital, Glasgow, Scotland.)

The authors present their experience using metoclopramide, in doses of 20 mg., intravenously as an aid in gastric emptying when there is delay whether due to gastric atony, pylorospasm or organic obstruction as in duodenal ulcer.

They describe their findings in the esophagus, stomach, small bowel and large bowel.

Most dramatic findings were in the stomach and small bowel, resulting in rapid evacuation of barium with associated simultaneous widening of the pyloric canal and dilatation of the duodenal bulb. Some patients had demonstrated lack of passage by the pylorus for as long as 2 hours after the ingestion of barium.

Eighty-three patients having follow-through small bowel studies were examined. The studies demonstrated that the barium tended to remain as a bolus and the passage of barium through the small bowel was much accelerated.

The findings in the esophagus revealed only slight hypotonia.

No specific action was found in regard to the large

bowel. Metoclopramide is used by the authors to examine the colon in an antegrade fashion, using gastrografin in patients who are unable to tolerate the enema procedure.

No action was detected upon the biliary tract.

The side-effects were confined to 2 episodes of sleepiness and 2 episodes of vomiting.

In summary, the authors present a pharmacologic agent to aid gastric emptying in those patients in whom delayed gastric emptying makes adequate examination difficult. No untoward side-effects have been discovered as yet.—*James Huddlestun, M.D.*

BAYES, BEVERLEY J., and HAMILTON, J. R. Blind loop syndrome in children: malabsorption secondary to intestinal stasis. *Arch. Dis. Childhood*, Feb., 1969, *44*, 76–81. (Address: Dr. J. R. Hamilton, Research Institute, Hospital for Sick Children, Toronto, Ontario, Canada.)

The clinical and laboratory features in 4 pediatric cases of intestinal stasis resulting in malabsorption and growth failure are presented. All were associated with congenital abnormalities of the small bowel.

The pathogenesis of the "blind loop syndrome" and its treatment in the pediatric age group are briefly discussed.

The authors stress the important association of congenital abnormalities with this syndrome in infants and children, and state that malrotation with duodenal bands is most frequently involved. They emphasize the need to be aware of the possibility of "blind loop syndrome" in children with abdominal distention and growth failure, and affirm the value of roentgenologic assessment.—*Victor G. Mikity, M.D.*

HEDDLE, S. B., PARROTT, K. B., PALOSCHI, G. P. G., PRENTICE, R. S. A., PERSYKO, L., and BECK, I. T. Diffuse eosinophilic gastroenteritis. *Canad. M. A. J.*, Mar. 22 and 29, 1969, *100*, 554–559. (Address: Dr. I. T. Beck, Associate Professor of Medicine, Department of Medicine, Hôtel Dieu Hospital, Kingston, Ontario, Canada.)

The authors describe a case report of what they consider to be the 36th of this form of disease and the first reported in Canada.

They differentiate the entity of localized eosinophilic granuloma from the one they describe as diffuse eosinophilic gastroenteritis, stating that the pathology of the 2 lesions is unrelated, the presence of tissue infiltration by eosinophils being the only factor in common.

In the diffuse variety there is often a family history of allergy and specific food intolerances or drug allergy. It manifests itself by recurrent abdominal pain, sometimes resembling partial small bowel obstruction. Physical examination is usually negative although there is occasionally ascites or signs of other allergic syndromes such as asthma. Laboratory examination shows a marked eosinophilia. There is absence of parasites and negative response to *Trichinella, Echinococcus* antigens, etc.

Roentgenologically there is narrowing of the pylorus and prepyloric antrum and thickening of mucosal folds in the small intestine. The combination of antral narrowing and eosinophilia should alert the radiologist.

Histologically there is eosinophilic infiltration of serosa, subserosa, and muscularis of the stomach and small intestine. In some cases this extends into the lamina propria. There may be a necrotizing angiitis of hypersensitivity type and eosinophilic infiltration of lymph nodes.

In establishing the diagnosis, it should be kept in mind that one-third of the cases fail to demonstrate definite pathology on peroral biopsy, and laparotomy may have to be performed.

The etiology of this condition remains unknown but it is theorized that eosinophilic infiltration of the gastrointestinal tract represents a somewhat localized allergic response to one of a number of nonspecific allergens.

In treating the disease an elimination may be tried at first and if this fails the use of steroids will usually cause a remission.—*Richard L. Bauman, M.D.*

MACKENZIE, E. A., ST. J. BROWN, B., and MANCHESTER, J. S. How far does the sigmoidoscope reach?—a radiologic evaluation. *J. Canad. A. Radiologists*, March, 1969, *20*, 20–24. (From: Victoria General Hospital and Dalhousie University, Halifax, Nova Scotia, Canada.)

The authors employed Michel skin clips to mark the distance of the bowel inspected. They found in autopsy specimens that the bowel could be perforated with the clips. They noted, however, that the best safeguard was to close the clips so that only 2 mm. separated the teeth before application. Hence, only a very small and shallow bite was taken in the mucosa.

The authors determined that in passing the sigmoidoscope to 18 cm., the instrument was at the sacral promontory. At 25 cm. the sigmoidoscope had passed well above the sacral promontory. They found that lesions above the midsigmoid can be visualized at sigmoidoscopy. There is a considerable telescopic movement of the bowel which comes down as a sleeve over the sigmoidoscope. They state that in their experience, the sigmoidoscope, being a straight rigid instrument, always records a level less than that actually read; thus, a lesion at 18 cm., while the sigmoidoscope may lie in fact at 30 cm. in the filled barium enema.

In the average adult the promontory of the sacrum

lies at about 18 cm. recorded on the sigmoidoscope.

In the individual patient, there is considerable change in position of the clips between the filled and emptied state of the colon. The greatest shift was found in the upper sigmoid and was in the order of 5 cm.—*C. Peter Truog, M.D.*

MOGUILLANSKY, PEDRO, and BURD, NATALIO. Colangiografía intravenosa y síndrome orgánico de Mirizzi. (Intravenous cholangiography and the organic syndrome of Mirizzi.) *Rev. argent. radiol.*, 1968, *31*, 154–156. (Address: Dr. P. Moguillansky, Radiodiagnóstico, Cipolletti, Río Negro, Argentine.)

The syndrome of Mirizzi includes signs and symptoms indicating obstruction of the biliary ducts; in the past this was attributed to spasm, inflammatory, or local organic lesions. In this report all patients had an organic basis for the condition.

The roentgenologic signs include incomplete obstruction of the common hepatic duct and increased opacification time indicating stasis above an area of obstruction. The patients may have episodes of elevation of bilirubin to such a high level that intravenous cholangiography is not successful. In this instance, one must wait for a time when the serum bilirubin is lower.

The common hepatic duct may be indented on the right by a distended gallbladder or may be involved by inflammatory changes secondary to gallstones. Calculi, fibrosis, or tumors may obstruct the distal common duct. Stenosis may also be caused by drainage tubes, ligation at surgery, hepatic cyst, parasites, and Hodgkin's disease.—*Charles M. Nice, Jr., M.D., Ph.D.*

VAN LERBERGHE, R., and LAURENT, Y. La cholangiographie par perfusion intraveineuse: étude de 103 cas. (Cholangiography by intravenous perfusion; a study of 103 cases.) *J. belge de radiol.*, 1969, *52*, 3–7. (Address: R. van Lerberghe, Clinique César De Paepe, 11, rue des Alexiens, Bruxelles 1, Belgium.)

Cholangiography with increased doses was performed in 103 cases, using 20 ml. of 50 per cent biligrafine plus 20 ml. of 30 per cent biligrafine, or in the obese patients the entire 40 ml. of biligrafine 50 per cent solution. The authors prefer 100 ml. of 10 per cent levulose as the diluent.

Four of the patients had reactions, all mild. Seven cases only had nonvisualization of the bile ducts; of these, 2 had elevated alkaline phosphatase, which may have been related to the failure to visualize.

The authors conclude that intravenous perfusion has three-fold superiority over the classical method: perfect tolerance; excellent visualization; and few failures, even in functional hepatic disorders as evidenced by bilirubinemia.—*Frank A. Riebel, M.D.*

BARRIGA, C. P., RODRIGUEZ, V. R., and WAUGH, O. A. Hepatografía por cateterización de la vena umbilical. (Hepatography by catheterization of the umbilical vein.) *Rev. argent. radiol.*, 1968, *31*, 131–135. (From: Instituto y Cátedra de Radiología, Prof. H. Cuevas R., Universidad de Chile, Hospital J. J. Aguirre, Santiago, Chile.)

Catheterization of the umbilical vein was attempted in 19 patients and successful roentgenologic examination of the venous drainage system in this area was accomplished in 13 patients.

After local anesthesia mid-way between the xyphoid and the umbilicus a median incision 5–7 cm. long is made in this location. Incision and dissection are carried down to the ligamentum teres or suspensory ligament of the liver. The umbilical vein still has a patent lumen in a high percentage of subjects. The vein is ligated distally and the lumen is probed with a dilator. A catheter is introduced and blood refluxes when the catheter reaches the portal vein. A heparinized 5 per cent solution of glucose is connected with the catheter and contrast material may be injected to study the portal venous system. After a test injection, 40 ml. of 50 per cent hypaque is injected with an automatic syringe at a pressure of 3 kg. per $cm.^2$ Six roentgenograms are exposed at 0.05 second intervals and 4 roentgenograms at 1.3 second intervals.

The umbilical vein empties into the left ramus of the portal vein in more than 95 per cent of the subjects.

This procedure is useful in the diagnosis of biliary retention and is superior to splenoportography in delineating extensive processes in the liver. The procedure is especially indicated in those patients in whom splenography cannot be done. These include: (1) Patients who have had splenectomy; (2) significant base pleural pathologic changes on the left; (3) hemorrhagic diathesis; (4) when it is difficult to locate the spleen properly; (5) tense abdominal ascites; (6) septic intra-abdominal processes; and (7) severe trauma.—*Charles M. Nice., Jr., M.D., Ph.D.*

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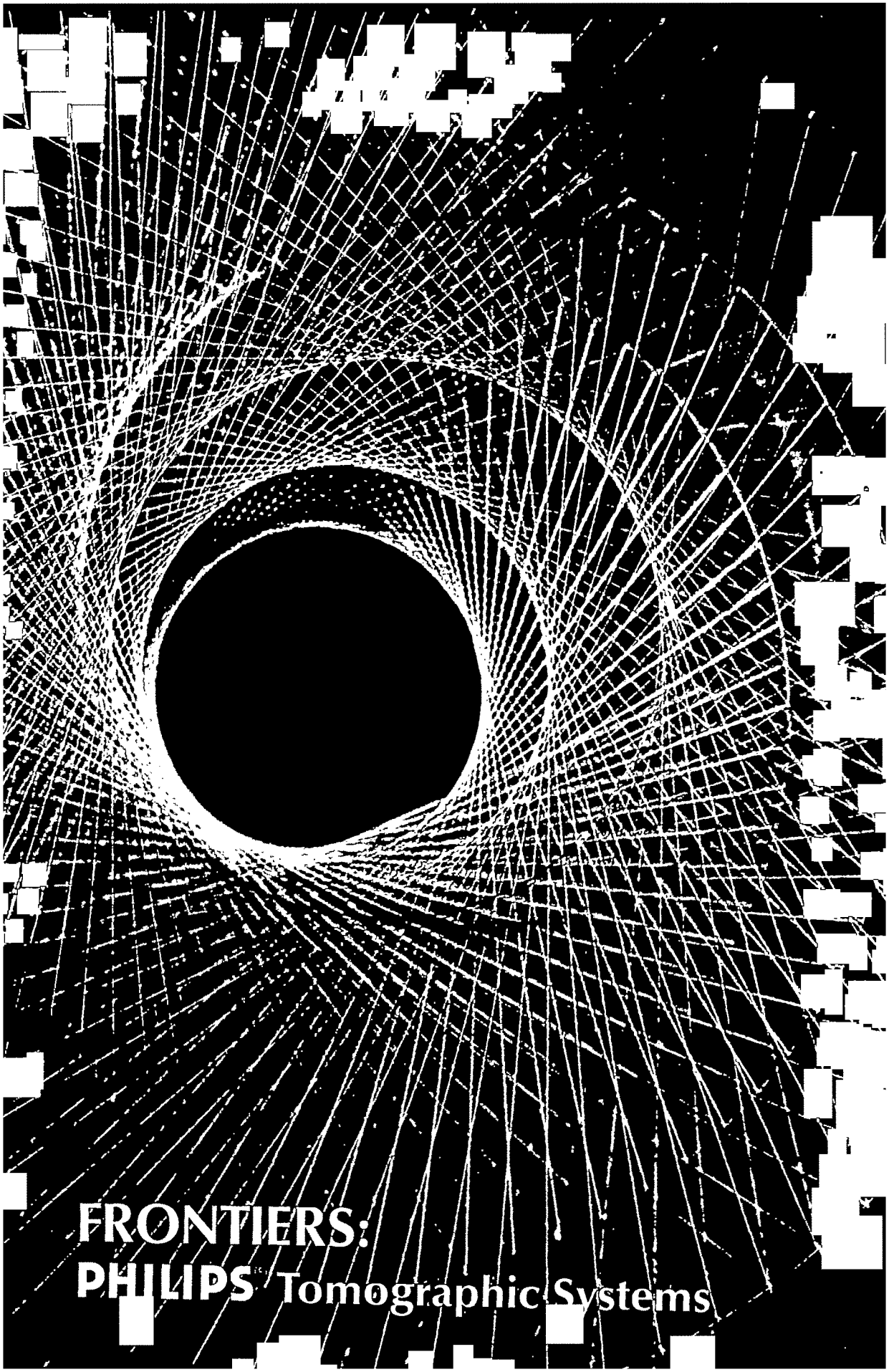
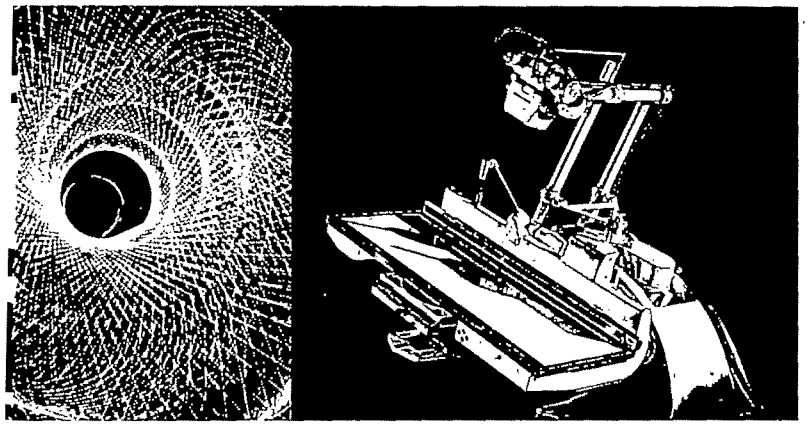

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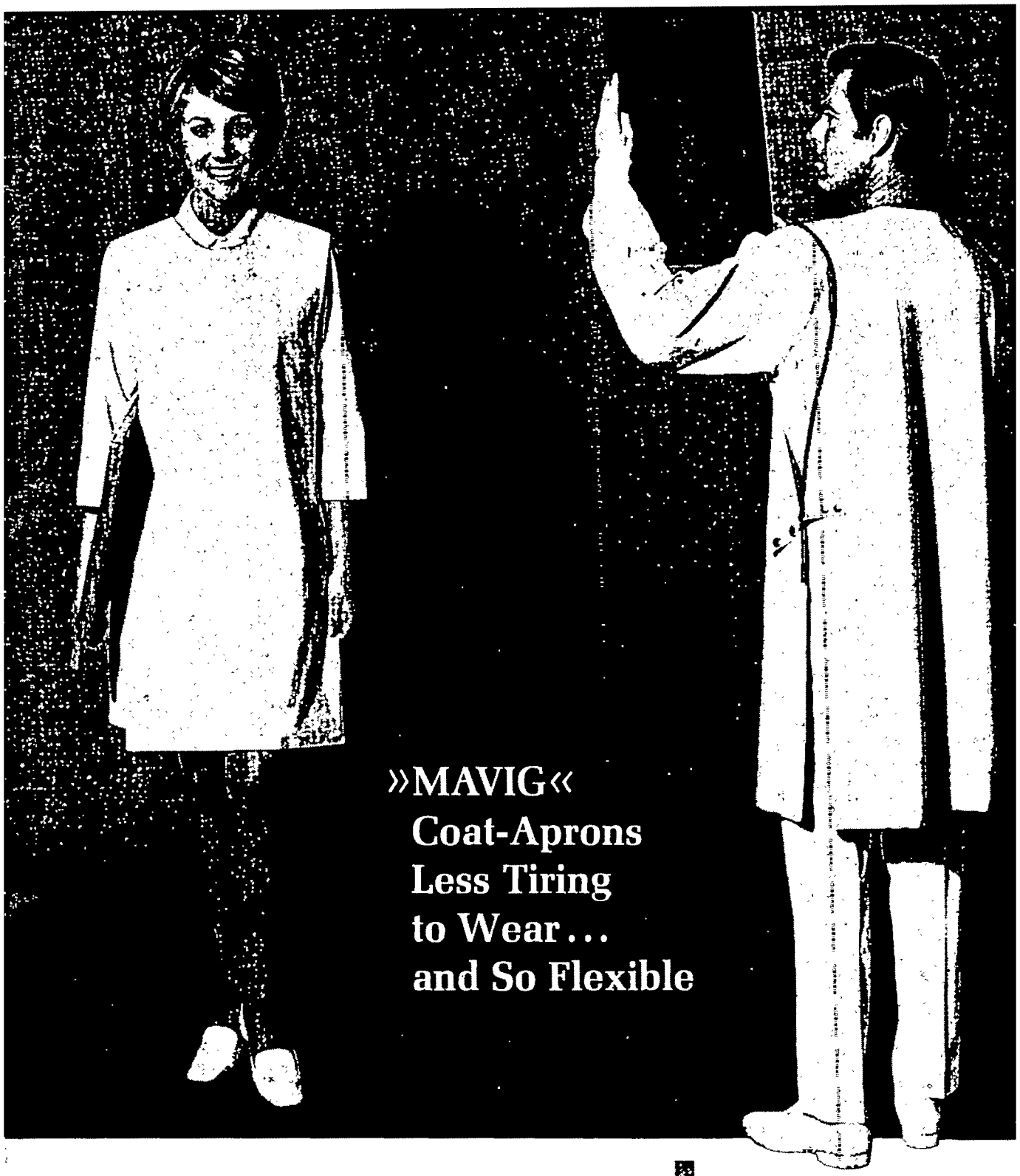
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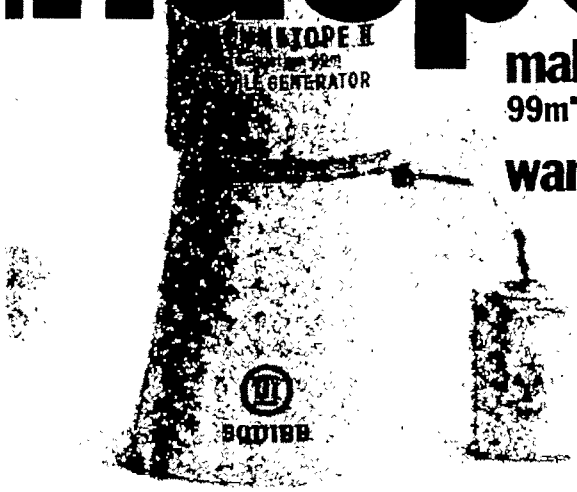
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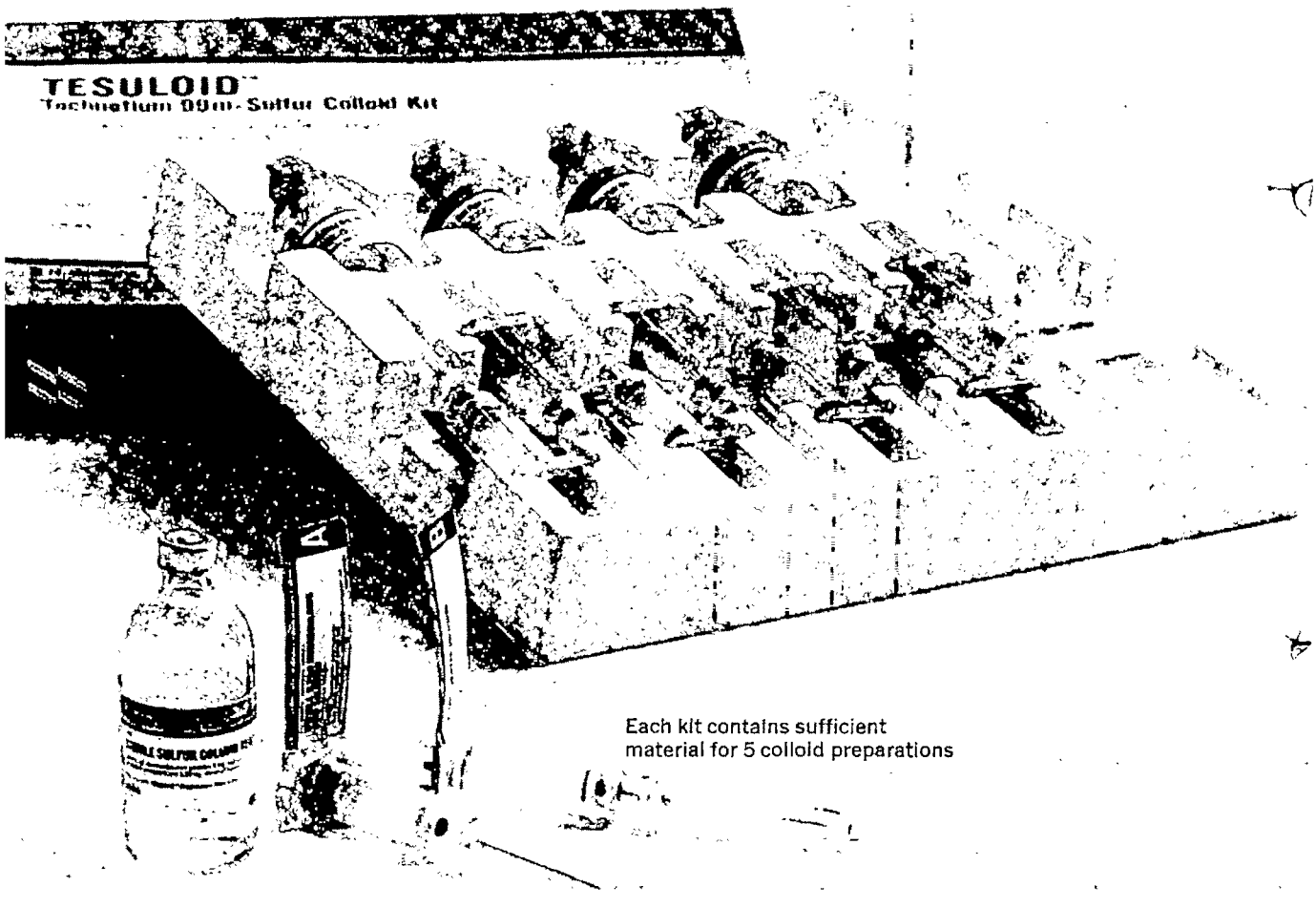
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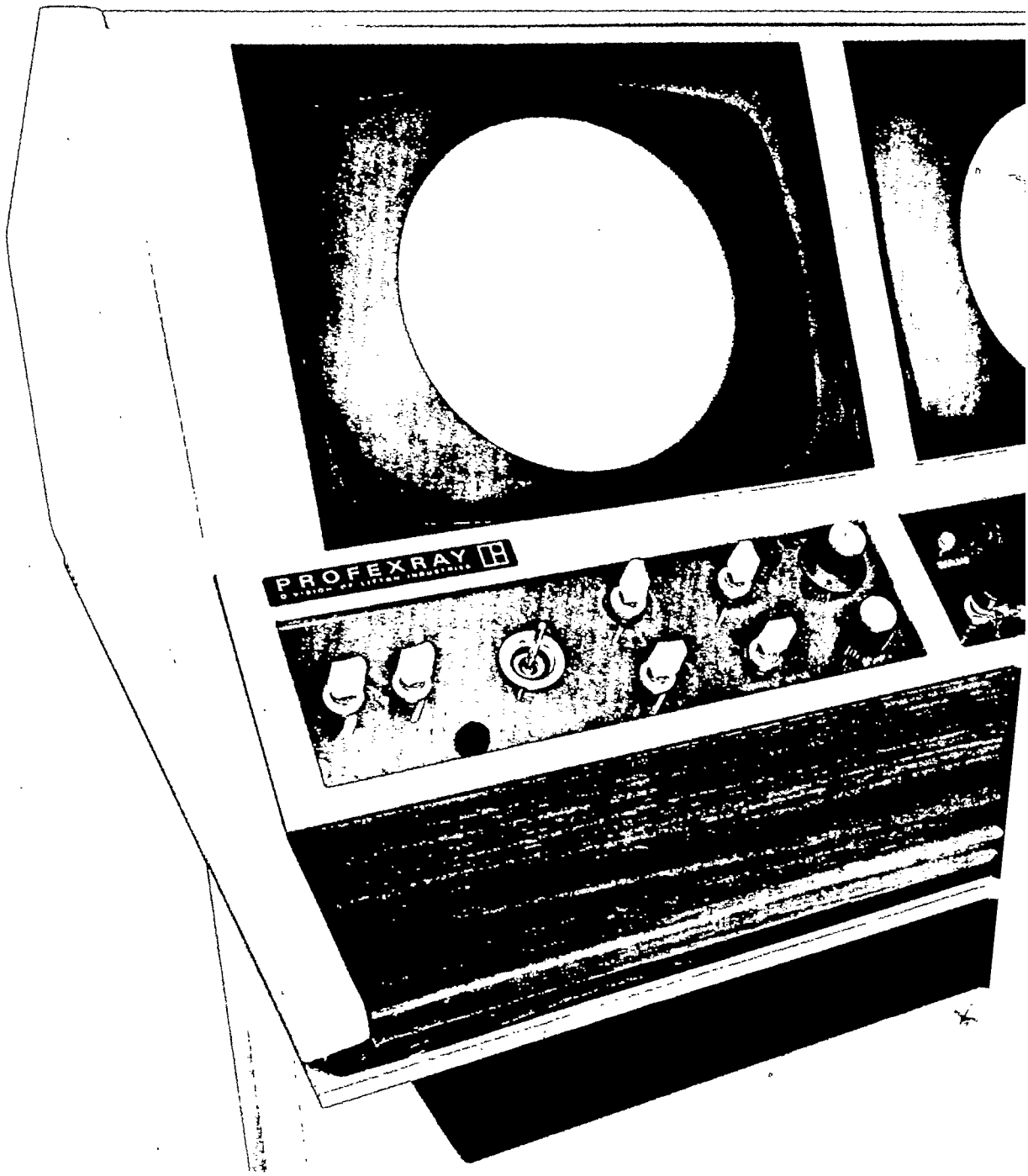
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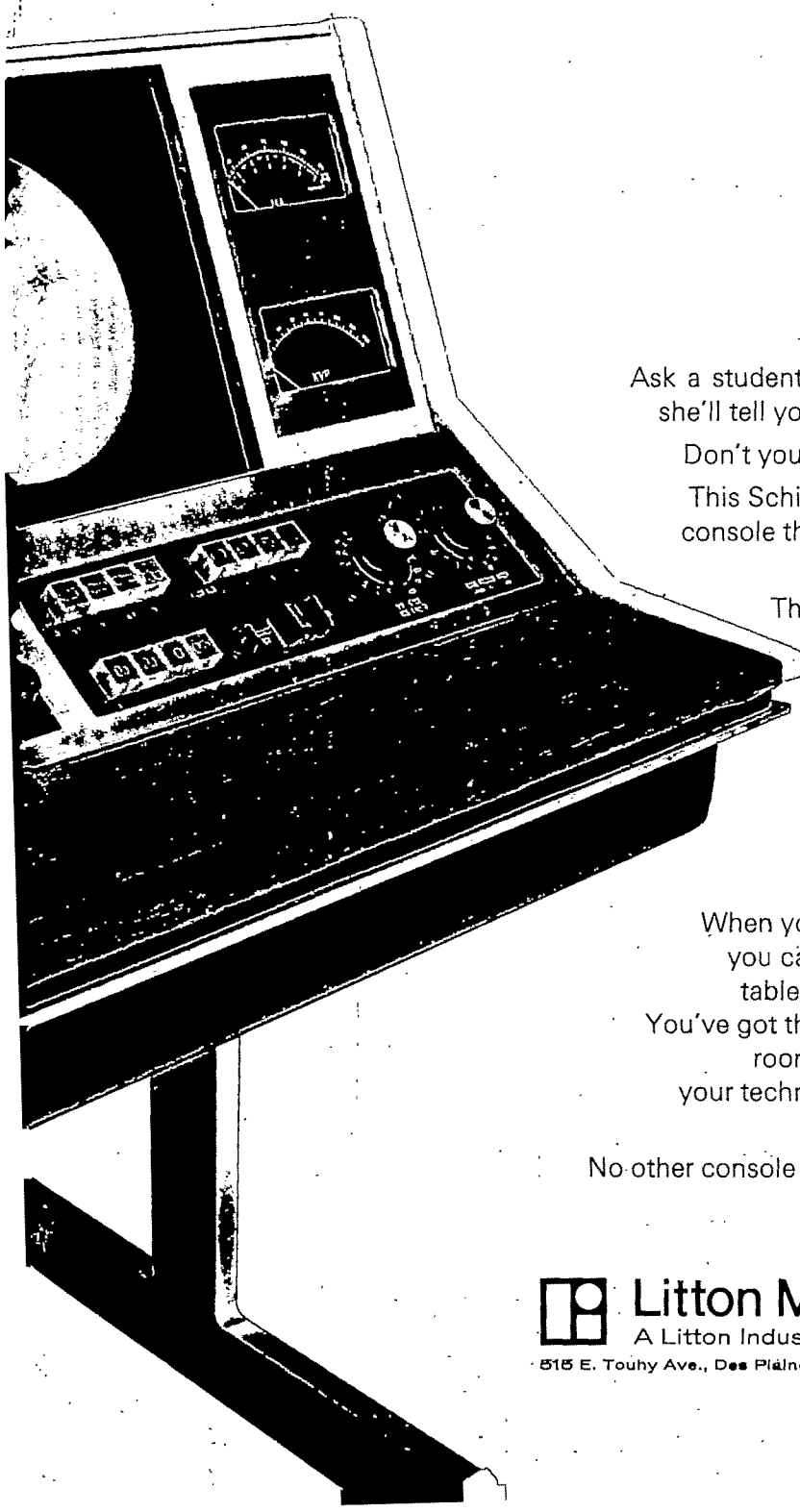
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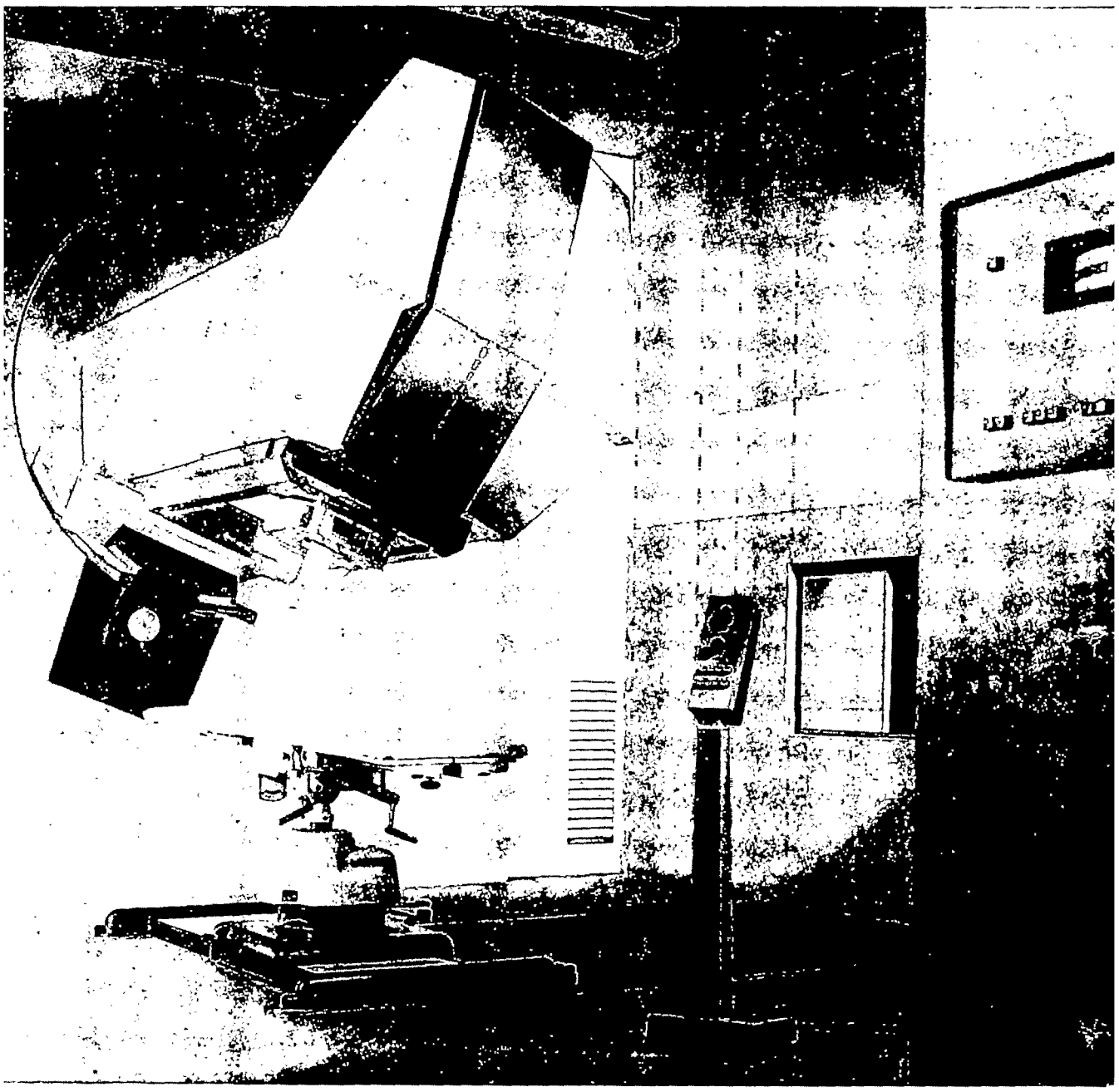
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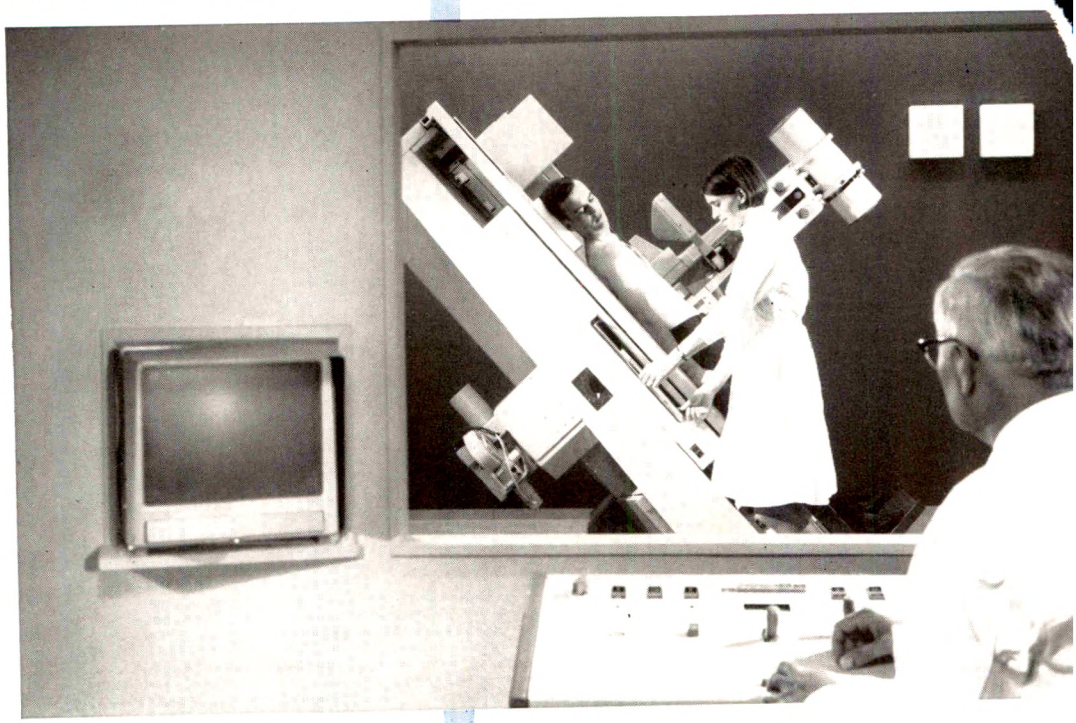
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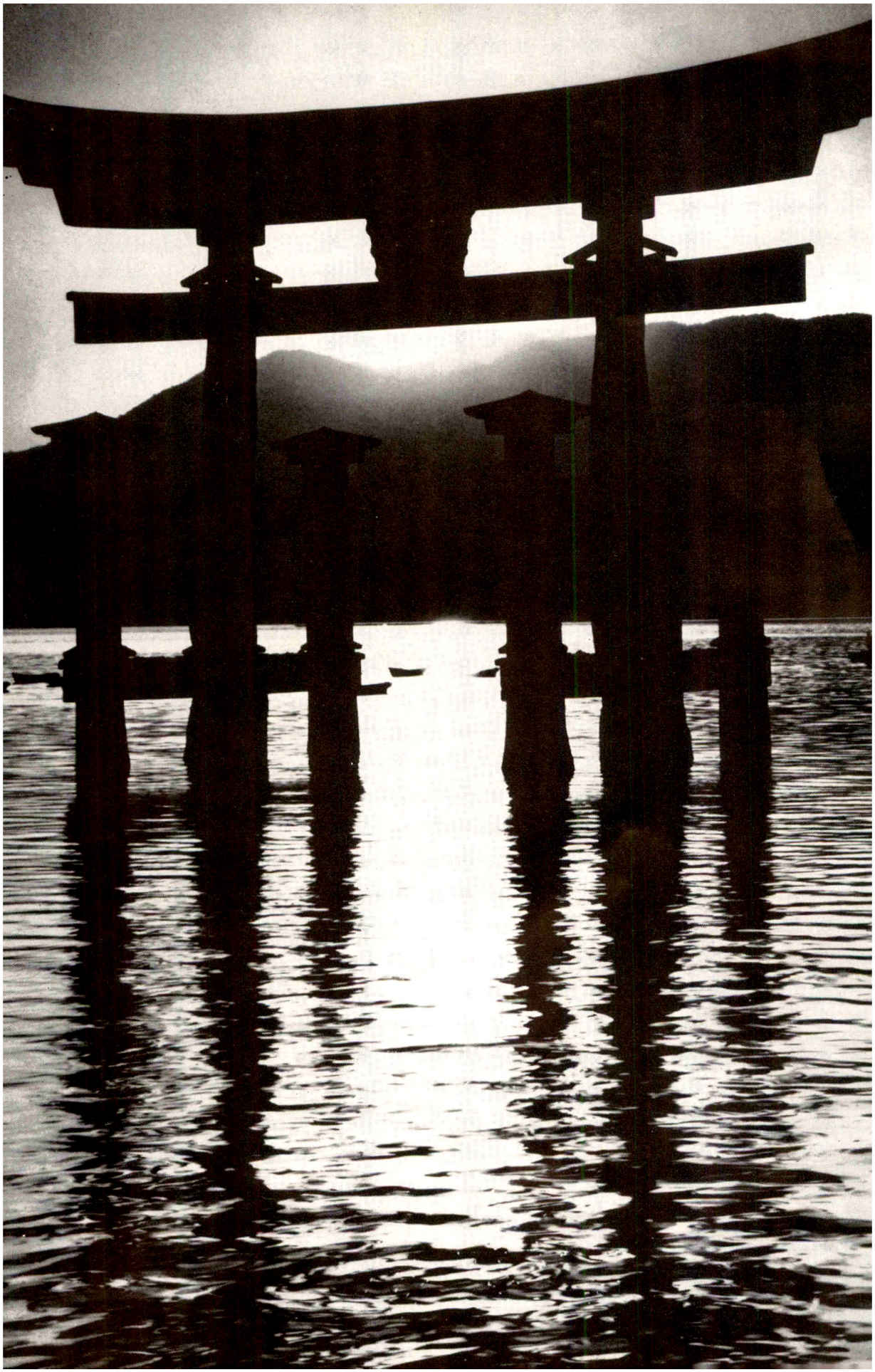
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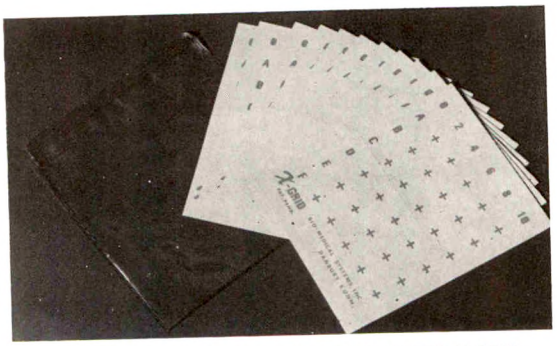
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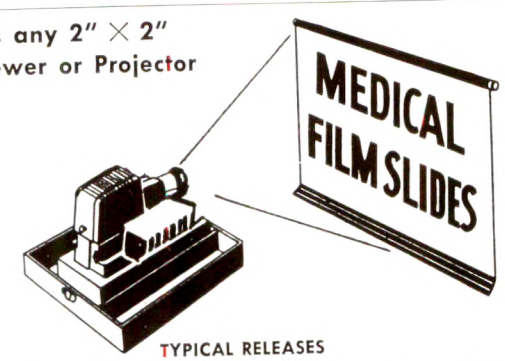
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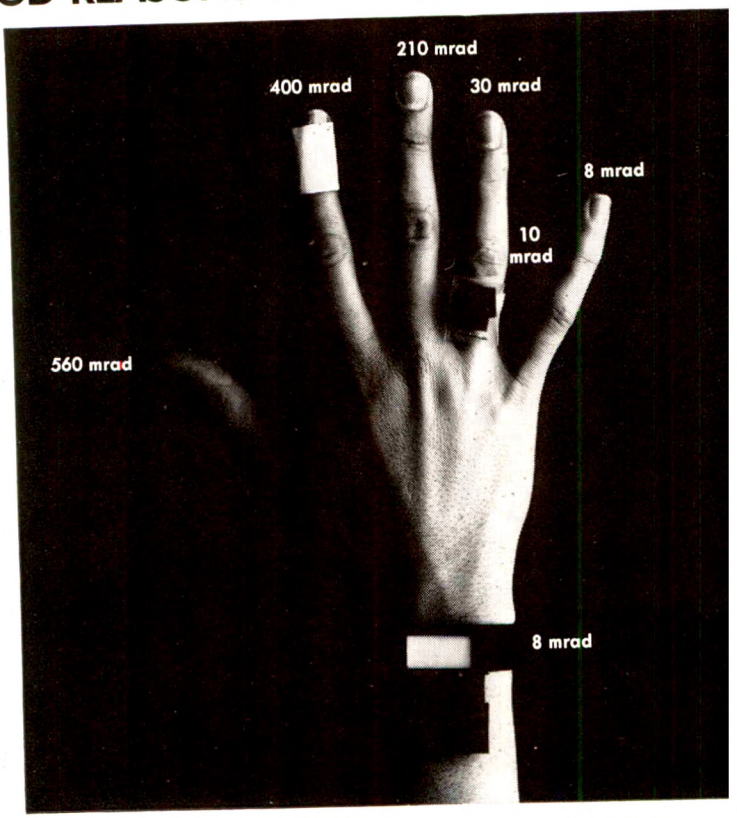
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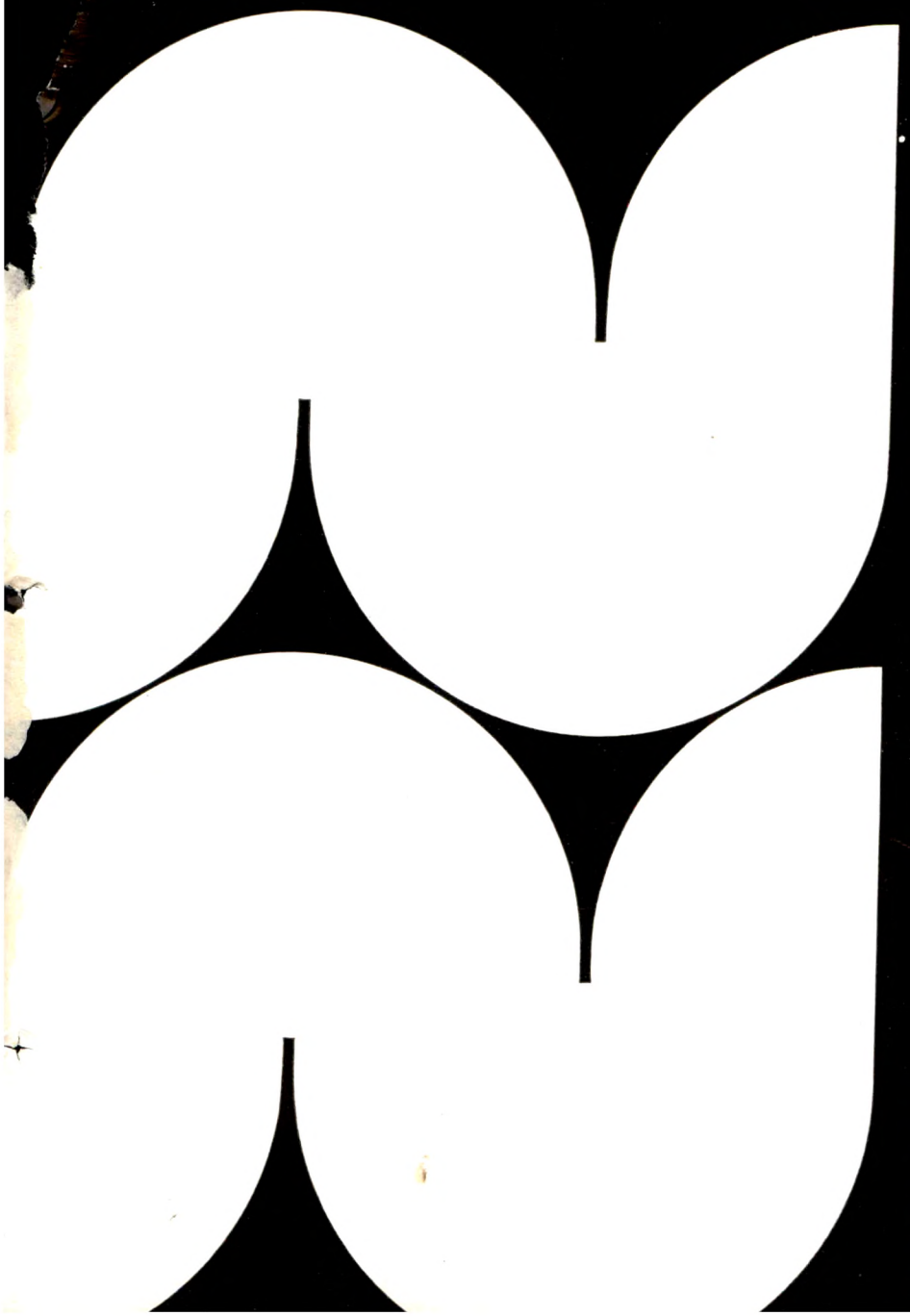
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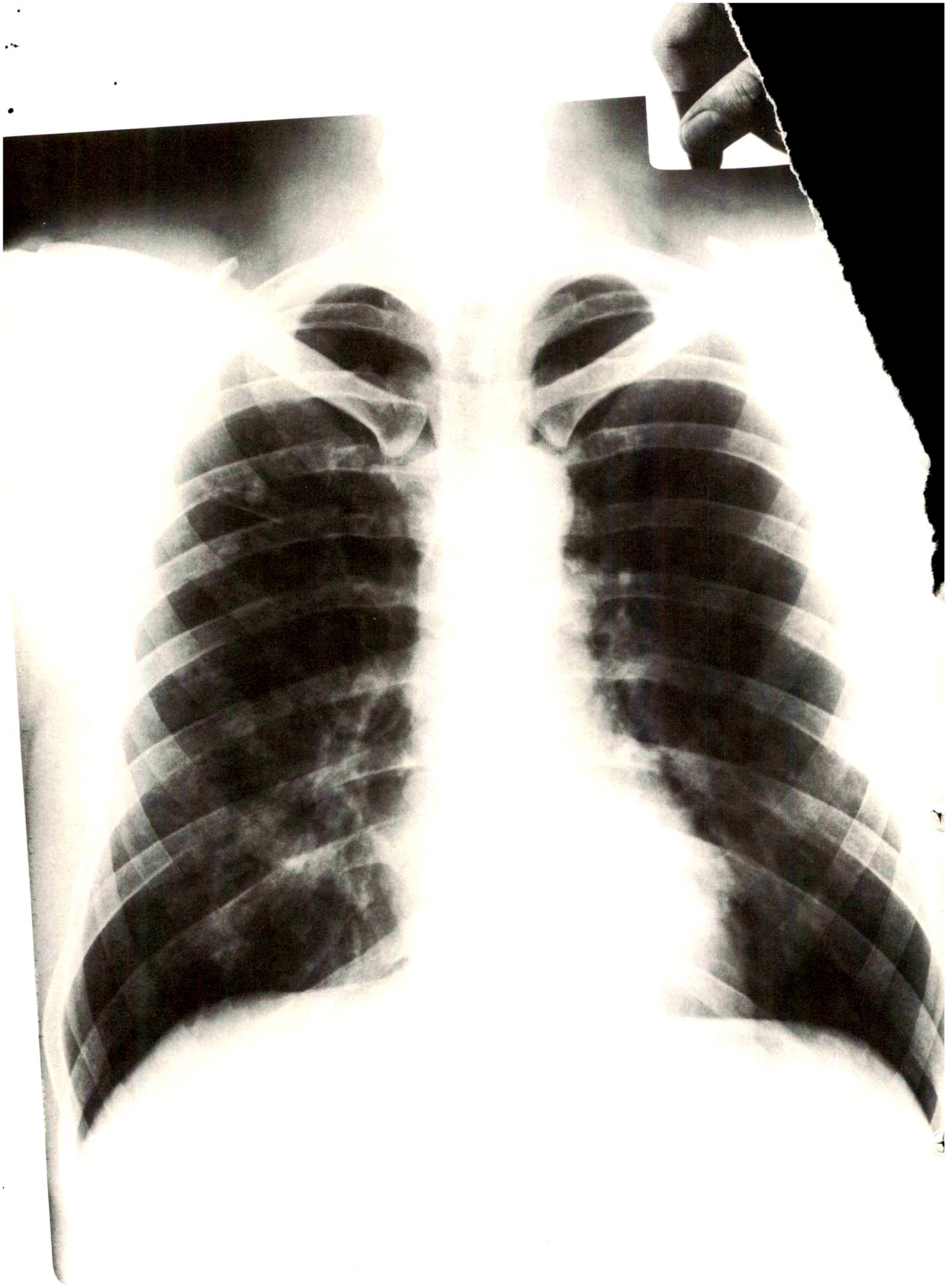
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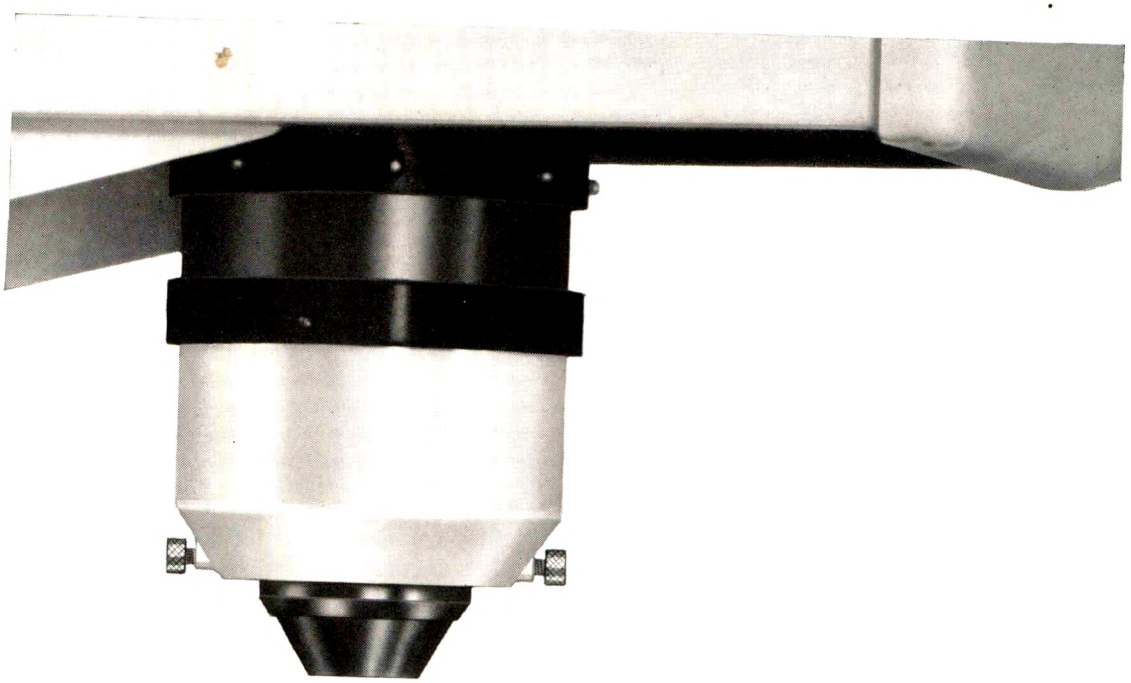
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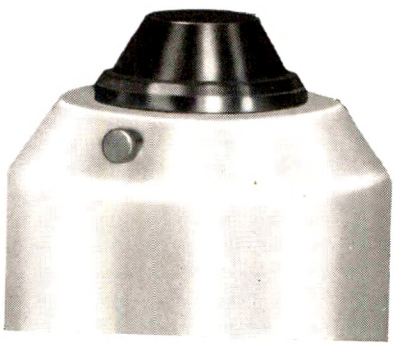
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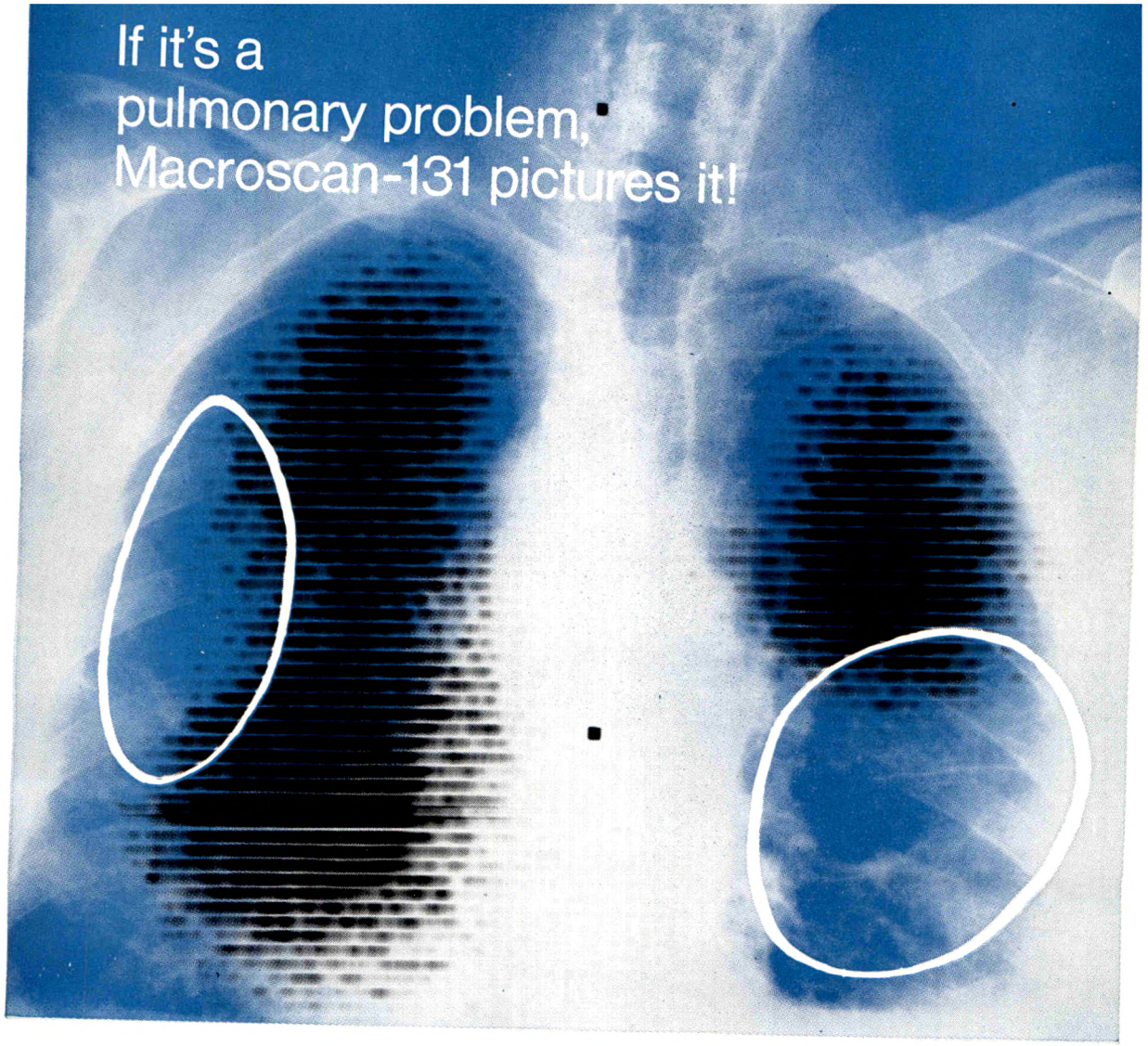
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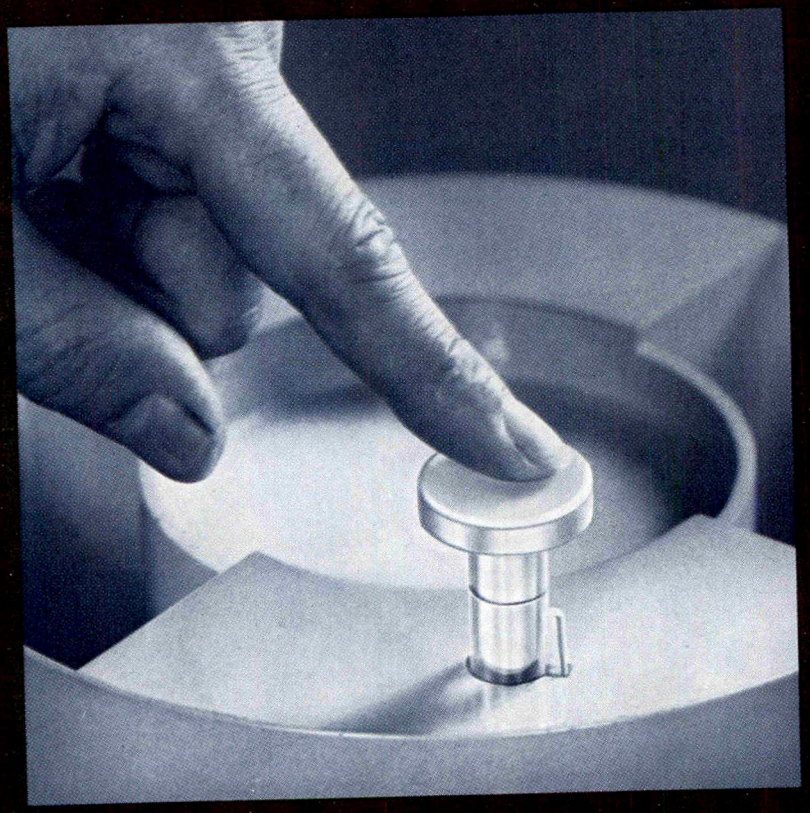
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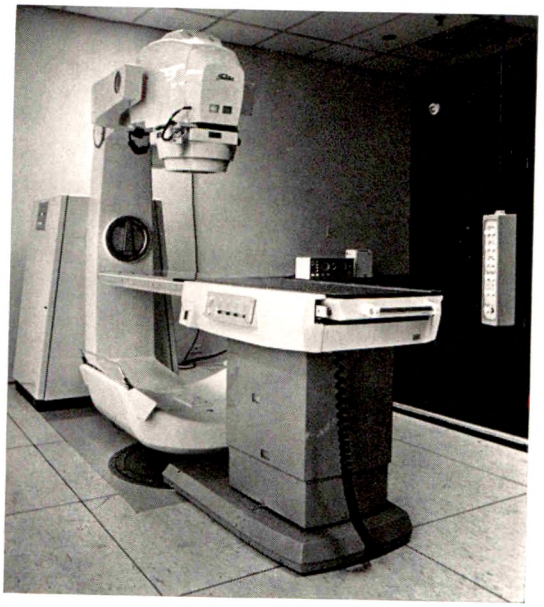
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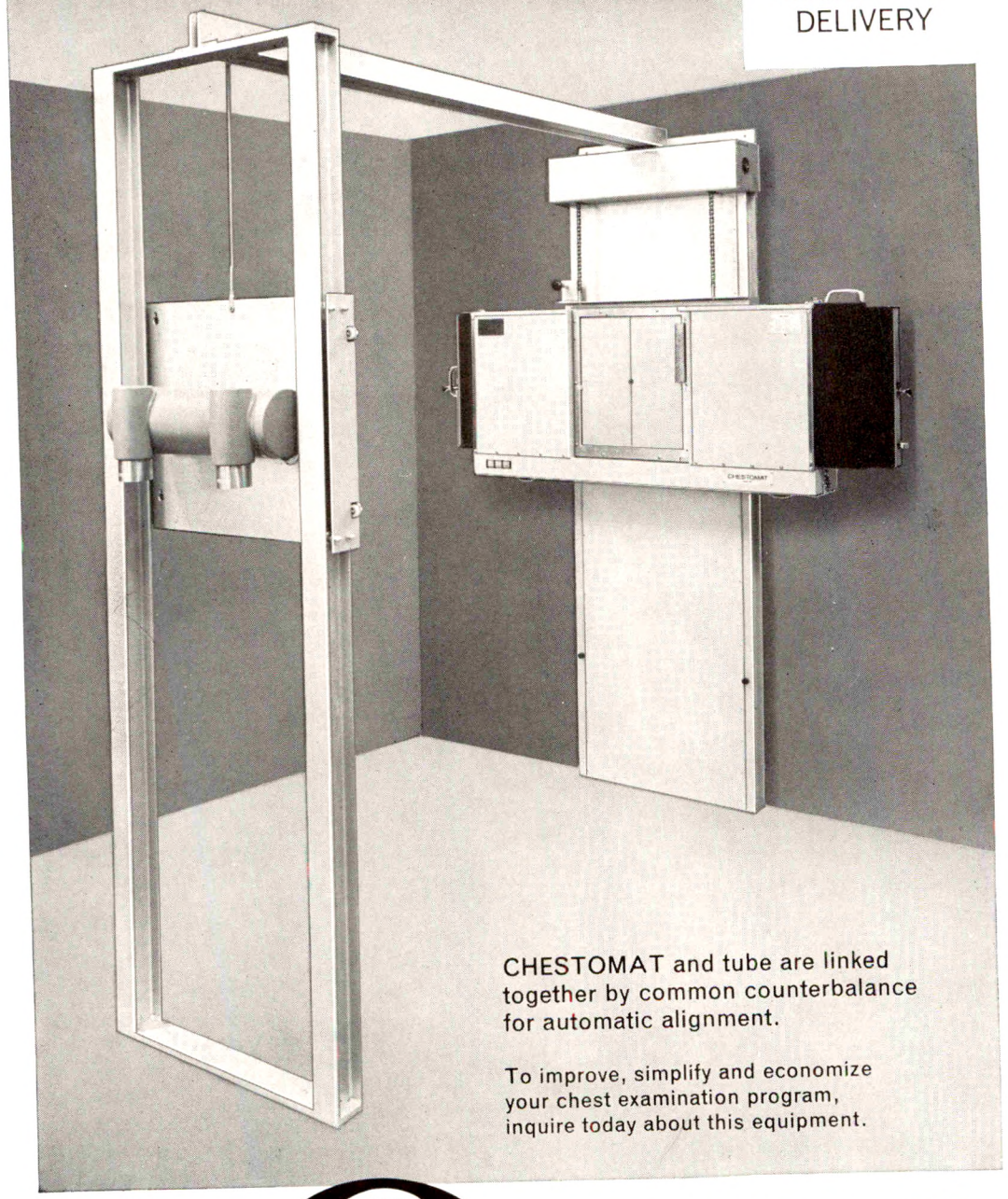
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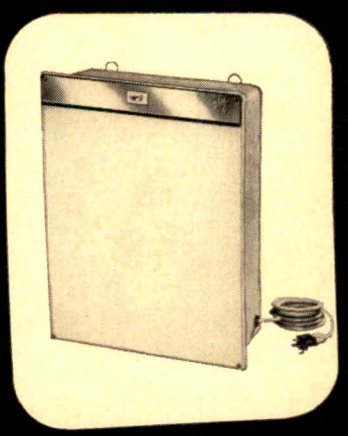
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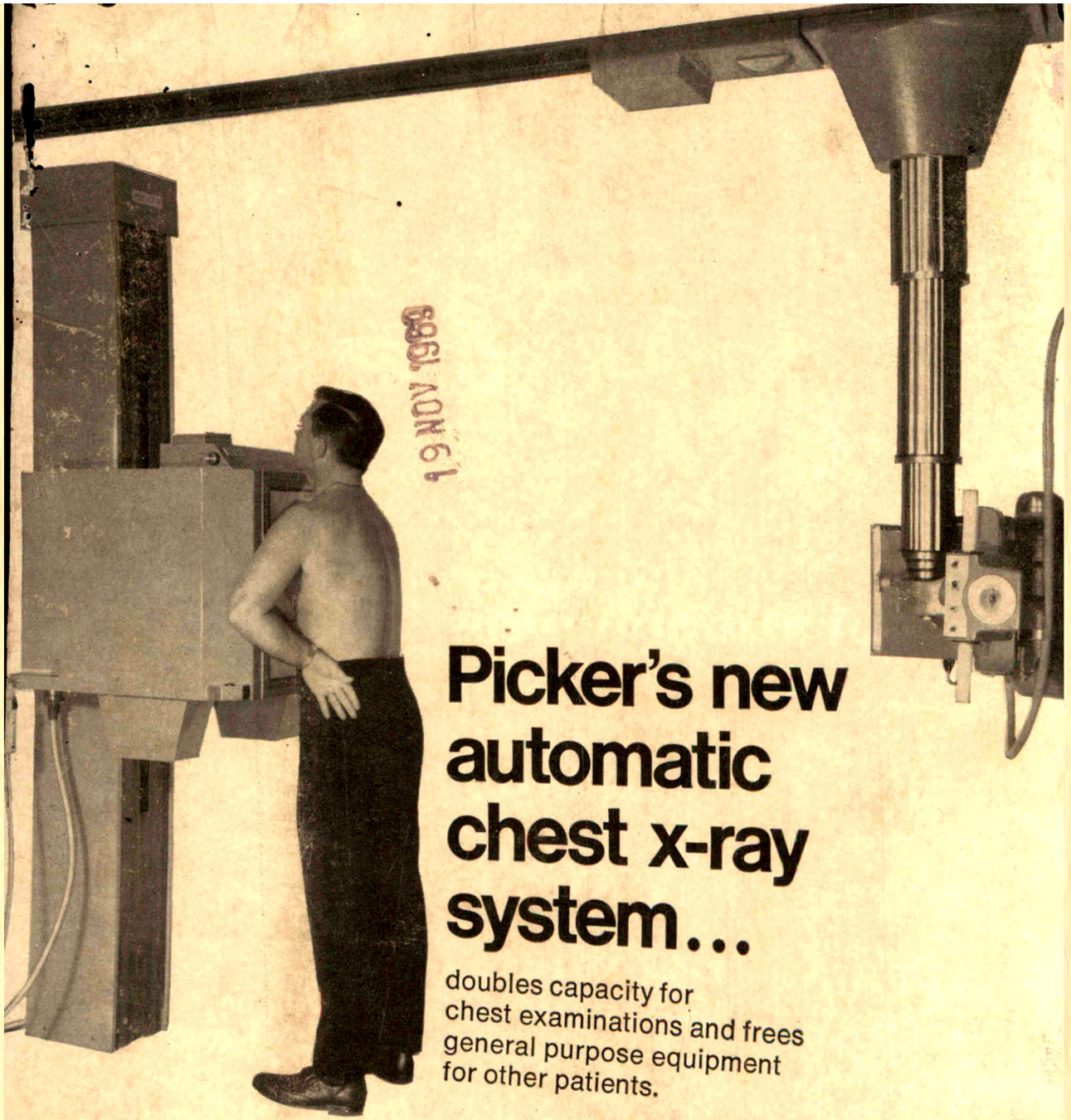


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The automatic film transport system moves the film from the loading magazine to the exposure chamber and then into the receiving magazine in just 3 seconds.

And finally: the insertion of the patient's ID card in the chest unit photographically imprints his identification on his radiograph.

To learn more about how our new system can double your capacity, see your local Picker representative. Or write to Picker X-Ray, 595 Miner Road, Cleveland, Ohio 44143.